"Life" shaped by genes that depend on their surrounds

Paul Gottlob Layer

Developmental Biology at Technische Universität Darmstadt, Schnittspahnstrasse 13, D-64287 Darmstadt, Germany

Manuscript to a lecture at the Workshop „Grundbegriffe einer Organismustheorie: Leben – Individuum – System“, on November 10-12, 2011, in “Hotel Kloster Johannisberg” (in parts published in German in Layer, 2007).

Abstract

Never was dogmatic reductionism helpful in conceiving the phenomenon of *life*. The post-genomic era has made it clear that genes alone cannot explain the functioning of whole organisms. Already each cell represents a unique, non-recurring individual. Recent progress in developmental biology has conveyed new perspectives both on the makings of individual organisms (*ontogeny)*, as on evolutionary change (*Evo-Devo*). The *genome* (the entirety of all genes) of an animal remains constant from fertilization onwards in each cell. The realization of genes requires *molecular environments*, in particular pertinent to the cytoplasm of the unfertilized egg. Individuality of an organism therefore is not only determined by its genome, but is shaped through developmental processes (it needs time!). Organisms can only exist through mutual interplays with their respective (molecular and cellular) environments at all levels of organization. Thus, *life* can be conceived of as endless networks of communication, e.g. as a mutual continuum, connecting all individuals, all species and all generations within their given environments. Evolutionarily, nature does not select *fitting genes*, but rather *viable traits*. The presented concepts render it unlikely that it was genes that founded our living world, but rather that distinct environments shaped “genes” (of whatever chemical nature) which proved to be “life-suitable”.

Introduction

Evidently, biology alone cannot give a comprehensible answer to the question of what is *life*, but it can only describe features of living beings (German, *Lebewesen*), e.g. organisms. Even in philosophy, the phenomenon of *life* remains a never solved riddle of reasoning. Robert Spaemann depicts a "drive-for-something" (*Aus-sein-auf-etwas*; Spaemann, 1996) as the determinative feature of living beings. A common theme of any organismic theory which tries to relate individuality with systems has to deal with communication. One possible approach to get an understanding of the various types and levels of communication is a developmental one: that is to follow ontogenesis from fertilization of a single egg through embryonic development until maturation of an adult organism. Such studies teach us that procedural advance of living beings depend at all possible levels - from molecular to ecological – on a pre-extisting vis-à-vis (*Gegenüber)*, e.g. the respective surrounds.

Social individuals: flocks of birds, of amoebae and of retinal cells

We watch a flock of birds: we see a first one, another one, then some more lift off from an autumn acre and nervously become air-borne. Hundreds and thousands of individual birds follow up into the sky. What in the beginning still appears like individual birds going each one on their own flight directions, very quickly the whole mass of birds coordinate their speeds and directions, to unite into a coherent swarm. It is a most fascinating scenery of watching nature in action: thousands of individuals moving in complete synchrony, but – looking closely with field glasses – each one individual still taking its own routes, keeping distance from its neighbor, shortly leaving the majestic general flow, and coming back into it again. What and where is here the individual?

Still watching nature, but this time under a microscope, staring into the world of unicellular organisms, or, protozoa, where the whole organism consists of just one (eukaryotic) cell. The amoebae *Dictyostelium discoideum* can often be found on rotten trunks of trees. These are organisms that under normal circumstances live as single cells, feeding on bacteria and dividing by normal cell division (*mitosis*). Like all amoebae do, they move around in all directions – for instance on a plastic dish under our microscope – and look for food. However, if food becomes scarce, we may watch how they quite suddenly begin to move concentrically

towards a central point. There, they do similar things as what our birds were doing after having lifted off from the ground, e.g. they unite to a mass of cells (we call it *aggregation*) which now begins to shape into one coherent body which people have come to call *slime mold*, the organism´s trivial name. This body of thousands of cells now goes through a defined life cycle, forming defined developmental stages of different shapes. Towards its end, spore cells are released which then live again as normal amoebae (under certain circumstances, even a sexual cycle can be included producing gametes). What and where is here the individual? Again, we can´t give a clear answer, but at least may ask, how these amoebae could make a decision so that all move towards one particular point in their two-dimensional world? The answer is that it was one particular cell sitting in the center spot which sent off a small diffusible molecule, which acted as the (alarm) signal telling everybody in the neighborhood to move together and unite. This example of the slime mold demonstrates that even individual cells are social beings, which hardly survive without communication with their comrades.

At least in multi-cellular organisms, there is no inner (internal) cellular life without an outer (external) one. Yet, how general is such a conclusion? A third example taken from our own research turns our views into an opened chicken egg (see Fig. 1, right) which has been incubated at 37 degrees for six days: we see the bended embryo with its huge eyes, we see even the lens, and translucent parts of the brain; lots of external blood vessels lead into the embryo´s body. Our experiment, with which we study the “behavior” of retinal cells within a culture dish, goes like this: from the isolated eyes we can easily remove the retinal tissue (the retina is the light processing part of our eyes) and disperse this tissue into single cells. From one eye, several millions of retinal cells can be regained. These cells are now cultured in plastic dishes, so that in a sense, they are now comparable to the individual slime mold´s cells. Rather than letting them sit down and let them move around, we now shake the dish on a rotation machine. What happens within the next couple of days is remarkable: the cells quickly reaggregate into little cellular spheres. These grow bigger, because cells still will divide. What at the beginning of reaggregation certainly still is a random assembly of different cells, after a short while begins to organize in space. After the spheres have reached a size of about 0.5 mm in diameter, we will cut the spheres open and apply different markers which reveal a pronounced degree of internal tissue organization. We find all types of retinal cells arranged in a retina-like order (Fig. 2): three layers of cell bodies are interconnected by synaptic layers. In other words, from an initial random agglomeration of cells, these millions

of cells – similar to what we have seen with Dictyostelium – have self-organized into a more or less complete tissue. Seemingly, our cells "talk" to each other, and find ways how to organize into a coherent tissue. In fact, we can direct these processes by changing the constituents of the growth medium, or change other parameters, showing that it is the environment which is constitutive to the development of this tissue. (Only as a side note, this methodology is what *Tissue Engineers* in these days apply to produce retinal tissue from stem cells in vitro (in the culture dish) to then use it for tissue implantation into diseased eyes; see Layer et al., 2010).

These three examples may demonstrate how difficult in biology it can be to define what individuality means, much depending on the level of observation.

Reductionists´ views on individuality

Ronald Reagan, by commenting on the last Sequoia trees in California *„…if you have seen one, you have seen them all"* intended to justify their final exploitation, but did not make himself more popular. Square-edged, as he was, he would not see the individualities of a tree, a look for the fine differences wasn´t his thing. Ernst Haeckel in the last third of the 19th century was a man who certainly looked at details. He much dug in the sands of the Baltic Sea coastline or at the Naples beach to find and describe new species every day, to the majority they were protista. He was most fascinated by the diversity and the beauty of their shapes, otherwise he would not have invested so much energy in making his famous drawings (Haeckel, 1998; Fig. 3). Besides presenting their novel forms, which were all unknown to the public, Haeckel certainly intended to visualize aspects of symmetry and regularities. Haeckel, like many other biologists of his time, pushed hard to shift biology into an *exact natural science*: quantifiable commonalities within the same species were in the show case, while their individual differences were neglected. He held to this principle, when – by going back to the work of Karl von Baer -, he prepared a famous picture (some say, he manipulated it!) with which he explained his biogenetic basic law: that ontogeny recapitulates phylogeny. He made some of the presented species and stages look more alike than they really were. Intentional fraud? I suspect that he was driven by his outspoken reductionism.

Blinding dogmas

August Weismann, another eminent German biologist of these days, became most influential by his germ plasm theory (*Keimplasmatheorie*). He could demonstrate in sea urchin that cells of the so-called germ line (*Keimbahn*; forming later all germ cells, e.g. eggs or sperm) are separated already in the very early embryo from what will become the somatic cells, e.g. cells that will form the whole body, except sperm or eggs. Being a follower of Darwin´s, Weismann thought about what the early segregation of germ and somatic cells could mean for the then much discussed question of heredity, e.g. how traits from one generation could be transferred into the next. His theory of heredity, which became also known as the "Weismann barrier", had tremendous impact on the conceptions of upcoming genetics in the first half of the 20th century. In his days, the nature of genetic materials, chromosomes, chromatin, nucleic acids, genes, etc., was still unknown, but it was assumed that there must be a chemical basis for heredity; some chemical units which somehow must be responsible for conferring specific traits to the animal. Weismann called these hypothetical units *determinants* (Fig. 4), and suggested that only cells of the germ line contained all genetic determinants. In some ways, a complete set of determinants in egg and sperm would be somehow mixed and worked over during fertilization, and thereby would reach into the next generation. In contrast, each somatic cell – which of course is also derived from a germ cell, namely the fertilized egg (*oocyte*) – would only receive a fraction of all determinants, depending on the cell type: a muscle cell would get one fraction of all determinants, a nerve cell another fraction, a fat cell again another one. Each particular fraction would specify the differentiation path of each cell type. From such ideas of fractionated heredity and cell specification, it was an expedient step for Weismann to come up with his concept of *mosaic development*. In essence, it assumed a one-to-one relationship between determinants (which later were called genes) and traits of organisms. Attempting to prove the mosaic concept would become the research program for a whole generation of embryologists.

By the middle of the last century, genetics had made tremendous progress. The nature of DNA had been solved (Watson and Crick, 1953), and the transfer of genetic information into chemical work machines of the body, the proteins, had been – as was believed then – fully understood: one gene codes for one protein (Beadle and Tatum, 1941), which became the central dogma of molecular biology (Crick, 1959; note: for more details on molecular biology, see Alberts et al., 2004). Dogmas in biology are dangerous, since they seem to advance progress; in the long run, however, they often retard it, since they direct our search of

knowledge (science) into wrong directions, blur our sights: what we normally could even see with our naked eyes, we then cannot perceive with the finest microscopes. Dogmas install belief systems. The danger of reductionism: to stumble upon your own dogmas. Both dogmas, the Weismann barrier as the Beadle-Tatum dogma turned out to be misconceptions: except for some specific exceptions, development is everything but "mosaic" in nature, and transfer of genetic information is everything but one-directional (from DNA to protein), nor is it one-dimensional (1 gene to 1 protein; cf. Fig. 1, left and Fig. 5).

A side glance on dogmatic evolutionary theory

These two concepts were particularly influential in the development of a "complete theory" of evolution, of Neodarwinism. What became known as *population genetics*, or *synthetic theory of evolution* was entirely based on these two dogmas of heredity and genetics: the complete set of genes, the *genome*, of a new individual becomes fixed at the moment of fertilization, and this *genotype* determines the future *phenotype* of this individual completely (Fig. 5). Ernst Mayr and Theodosius Dobzhansky as eminent masterminds formulated "*The individual mutates, the population evolves*" (Amundson, 2005). Since only mature reproducing animals would affect the process of evolution through natural selection, population geneticists did not care about the embryo. Since supposedly the phenotype reflected the genotype directly (and vice versa, 1:1, Fig. 6), it was assumed that natural selection would work directly on genes. In fact, population genetics is nothing but statistics on the fitness of individual genes (and thus reflecting the traits, - as it was believed -) in a given population. What a misconception: as if nature would select for fitting genes? If anything, nature selects for survival for "life" (of whole viable organisms). It was Ernst Mayr who did not allow embryologists to participate in his conferences on population genetics, since he trumpeted that embryology could not contribute to the understanding of evolutionary process. Wrong dogmas will fall at some time, like the Berlin wall. From the late eighties onwards, *Evo-Devo* (evolutionary developmental biology) has become the field to explain on a molecular basis how big changes of biological form can come about during early embryonic development (by spontaneous mutations, e.g. by environmental toxicity, stress, etc.). If this animal can make it to maturity, it may possibly reproduce and even install a new population: a step of macroevolutionary change may have happened. The big dilemmas that population genetics had left open were characterized by Ron Amundson when he says "Evo-Devo and population genetics are incommensurate. One or

the other has to disappear, before a new synthesis (of evolution) becomes possible" (Amundson, 2005; see also Gilbert, 2010).

New sights from embryology on individuality, environments and genes

Since the times of Weismann, people could have known better. Dogmas kill fantasies, and the phenotype is not a mere reflection of the genotype. It was Hans Driesch, who like others, set out to prove Weismann´s mosaic concept. Instead, with his famous *Schüttelversuche* (rotation experiments; see Gilbert, 2010) he found the opposite. When he had dissociated the four-cell embryo of sea urchins into its four cells, he had expected to get – if anything – four different sectors (parts) of the developing animal (remember the idea of a mosaic!); instead he observed the formation of four little, but whole and viable sea urchin larvae. In other words, from each cell (out of four) a complete animal had developed. Quite shocked by his own findings, he stated "the prospective potentiality of each cell is larger than its real fate". With this experiment, by the way, he had detected *totipotentiality*, and thus became the father of nowadays stem cell biology. What cells, and what organisms do, depends not only on their given genome (which is the same in each cell), but depends on their pertinent "life conditions", their environments (or what we call in German, their *Umwelt* – lit. *"surround world"*).

The great surprise from genomics: much animal from few genes

A complete change in the perception of genetics came about after genomes of many animals, including man, were resolved around the turn of this century. It came as a big surprise that the numbers of genes from worm to the fly and then to man did not differ dramatically. Furthermore, many important gene families are preserved in the entire animal kingdom (and even in all multicellular organisms), and were conserved throughout evolution. Our genetic identity with chimpanzees is higher than 98%. How closely related with each other are the members of a human family? We can detect their similarities by their looks. But still, how different are they by their characters, their behaviors, their whole personalities? What part plays genetics, what their environments for each of these persons?

On impotency of genes: they need an environment

Living in the era of informatics and genomics, the media still often convey the impression of genes being almighty, omnipotent agents, being placed at the uppermost peak of an organism´s hierarchies. It seems bad luck if you have gotten the wrong genes: instead of becoming a winner, a brilliant star, you end up as loser, an alcoholic, or a criminal. There are brain scientists out there who try seriously to convince our law makers to change laws accordingly, since it is argued that there is no true human free will but mere genetic predisposition. Since it was your pre-determined genetic disposition, you cannot be made responsible for whatever you are doing right or wrong in life. How wrong a conception of the impact of genes!

In order to understand what makes all cells of an organism alike, but at the same time also different, we have to deal with the omnipotency, but also with the helplessness of genes. From two similarly looking egg cells two very different organisms can originate, e.g. a sea urchin or some frog. Through fertilization of an egg by the sperm maternal and paternal genes are mixed, forming the genome of the new individual. How will the information that is encoded in this new genome be realized? Briefly some important facts: in each cell of a given organism (e.g. a growing sea urchin, or a human fetus) the genome, as it was mixed together at fertilization, is completely preserved in each and every cell of the growing body. Therefore, we can speak of *genomic constancy* in all cells within any individual body (with some exceptions). But if the genetic program is the same in each cell, how then is it possible that all the different cell types can be formed during development? To understand this, we have to deal a bit more with the realization of genes. Leaving off any details it should be noted, that there are regions on the DNA which function as switches to turn genes on, or turn them off, respectively. Thus, to transfer the information of a gene into its respective protein (e.g. to "realize" it), a particular gene must be activated. Importantly, the gene´s activity must be regulated in time and space: it should be produced only where and when this protein is needed (e.g. should its gene be "ON"). This is what molecular developmental biologists call *differential gene expression*. Thus, each cell of our body contains a complete set of the genetic information (the genome), but in a given cell at a certain time by far not all genes are active; to the contrary, most genes are inactive, remaining quiet for most of the cells life (here, mechanisms of *epigenetics* are left out!).

A second question arises immediately, namely who or what serves at those switches? As little as we cannot pull ourselves out off the moors, so a gene cannot activate or inactivate itself. Instead, there are proteins, called *transcription factors*, endowed with this function. Often, such factors turn on their own production (Fig. 1, left). Engineers reading this will immediately notice that this will lead to feedback loops and action cascades. A continuous chemical mutual interplay between genes, their proteins and other genes eventually leads as a consequence of the sum of these endless chemical reactions to a living organism. Synoptically, to build an organism, it needs many genes and proteins; development is steered by differential gene expressions; genes themselves represent only "dead chemistry", since they need to be activated; each protein has to be at the right site at the right moment; strong feedback means that proteins often regulate their own production, and that of consecutive genes (called *down-stream genes*); by such mechanisms lead to genetic cascades, e.g. gene 1 codes for protein 1, which in turn regulates gene 2, etc. (Figs. 1, 6).

The genome as origin and ruler of individual life?

After this short side view into how genes are realized, we can come back to our central question on the origin of individual life, how embryonic life begins. For instance, how is it possible that from the genome of a fertilized egg a fly with wings, legs, antennae, etc., can develop. This is a most complex issue which has fascinated man since millenia. Over centuries of scientific reasoning, the so-called *preformationists* never completely disappeared, believing that in the sperm´s head an entire little human being would be present as a preformed *homunculus*, which then only needs to be unfolded and enlarged in the maternal uterus. Our novel molecular insights into these processes show that it is *epigenesis* (development), rather than *preformation*, as Aristotle already rightly had supposed.

Transgenerational aspects of individuality: before something new comes into being, something must be there already (maternal prepatterns)

Commonly, we are often given the impression as if the newly combined genome which emerges by combination of both parental genomes, would solely and completely be responsible for the development of the organism from its moment of fertilization until adulthood, as comparable for instance with the might of a general who autonomously can

command and direct completely all war activities. Such an impression is not entirely correct. In particular, the very earliest periods of individual (embryonic) life appear to depend decisively on conditions as existent already in the unfertilized egg. These still relatively novel insights shall be discussed by using the fruit fly as an example. Not being understood to the same degree for man, we can expect that so-called *maternal factors* play a similarly important role during human development.

How does earliest development take off in the egg (Fig. 6)? The great research achievements by Christiane Nüsslein-Volhard and many others have taught us the essentials (Nüsslein-Volhard, 2004; Gilbert, 2010). *The egg is not round* could be a subheading for this section, indicating that the egg during its production in the womb not only reaches a certain egg-like shape ("un-round", not perfectly spherical), but also takes on molecular asymmetries. Some important molecules (factors, morphogens) become amassed near the front (anterior), others near the hind (posterior) pole of the egg. The bright red dot in the figure (Fig. 6, I) indicates the concentration of a so-called *bicoid* messenger RNA at the front pole of the flie´s egg. This mRNA is deposited there by the mother fly during egg production; we speak of a *maternal,* e.g. by the mother produced mRNA. Immediately after fertilization, but only then, this mRNA is translated into its protein. This protein also presents a distinct front-hind distribution, forming a gradient throughout the length of the egg (graded red dot in II. of Fig. 6). The *bicoid* protein acts as a transcription factor, then activating (together with other factors) down-stream genes, thus initiating gene cascades (Fig 6, III., IV.). Noticeably, these reactions are concentration-dependent: only at places where enough of *bicoid* protein is present, a certain reaction is initiated; at places with less *bicoid* other things may happen. The cascades which will follow have been characterized in much detail, but need not be outlined further here. Nonetheless, we now can understand how molecular patterns are generated at distinct regions of the newly forming organism through stepwise genetic cascades and repetitive feedback mechanisms. By these processes, first irregular stripes (Fig. 6, III.), then double segments (Fig. 6, IV.), segments and eventually distinct cells become molecularly determined. Each molecular sub-pattern can produce certain structures of the growing larvae, until the mature state of the fly has been reached, e.g. a head, trunk, a segment, antennae, or legs.

What have we learnt? It is not only the "naked" genome of the future fly which produces it (quasi from nothing), but it is *the already existent molecular surrounds within the unfertilized egg which directs early steps of the individual´s pattern formation*. Without such an initiation from offside of genes no development of the fertilized egg will even set in, the genetic

material will remain quiet, simply speaking: the fly will not develop. To say it blankly, genes themselves are as mute as a software in a computer which is not activated (we open the software "word" to work on a text; to do table calculations we will use another program). Thus, we learn how the emergence of a next generation is decisively directed by factors from the egg, and thus from the mother animal (this is a crude simplification, not further touching maternal and paternal influences). The transition from one generation to the next is therefore – to my understanding – much more fluent, since the *new life* not really is new. What – then - means *individuality* at the organismic level?

No doubt, to form a new organism the fertilized egg must use the information laid down in its genome. With this business, however, it is always the already existing environment, or, surrounds which plays a major part. The term "surrounds" could mean the surrounding molecular composition (a particular transcription factor, a hormone, etc.). But similarly, gene expressions can be influenced by the wider surrounds, such as conditions within or outside of neighboring cells at a given moment, of whole tissues and organs, or even whole organisms with their respective food supply, conditions of temperature and light, or outbreak of diseases (thus, "surrounds" indicates all scales, from molecular, to cellular to organismic; I prefer the German term *Umwelt*, which by including "Welt - world" can nicely insinuate a scalar openness).

Back to Haeckel: on symmetries, networks and system levels

In doing biological research, we always end up by being struck by the complexity of biological systems. As with all natural sciences, we biologists have to strictly work and reason reductionistically. At the same token, since biology deals with most complex natural matters, one should refrain from interpreting results, which are due to reductionistic methodologies, in a dogmatic manner. There is not much of a "proof" in biology. While Haeckel and his contemporaries were trying to point to regularities and symmetries in nature at the species level (reductionist approach), nowadays we have come to focus on individual features of molecules, cells, tissues and organisms. We could consider *individuality* at each scale, and this multileveled nature of the term *individuality* has been highlighted to some extent in this article (see also contributions of Nick and of Bereiter-Hahn, this volume). The term *system* in biology is even more iridescent. Like that of individuality, systems can be designated at all levels, from three molecules being dependent on each other within a chemical reaction

scheme, up to complete organisms, of which already very few –by depending upon each other - can form an ecological unit. Almost endlessly, all these possible systems are interconnected with each other. It is the modern field of *Systems Biology* which tries to describe relevant networks (which are always parts of other networks) by computer-assisted simulation approaches. Since they all include simplifications, they are all error-prone. Nevertheless, we hope that they can further our understanding of the living world.

At higher levels of organismic life it is by far not only genes which rule the game of life, but rather systemic rules take over (constraints). Cells, tissues, organs, organisms do what they are capable of doing in a given situation. A neuron sends out his processes into such directions which are indicated by the make-up of its environments (e.g., particular molecular guiding cues provided by the ECM). If dissociated retinal cells find together in a rotation culture, they produce a coherent tissue by following many diverse cell-internal and external cues (molecular, cellular surfaces, physical constraints, such as tension or pressure, etc.). The list of examples is endless.

Why do mammals have always (with very few exceptions) seven neck vertebrae? If we think of a giraffe, this seems not a helpful invention of nature. Why does this animal not have many more which would make his neck much more flexible, and thus could be an evolutionary advantage? In fact, sometimes researchers find mammals with one more, or one fewer vertebra (even in man). Surprisingly, at a closer look it could be established that such "malformed" individuals either die early, or they will develop cancers. For unknown reasons, which we call "systemic constraints", mammalian life appears only compatible with having precisely seven neck bones (Arthur, 2011).

In contrast to Haeckel´s impressions, symmetries in living organisms are deceivably pretentious. Truly, it is asymmetry that drives life. A remarkable mathematical approach to understand the formation of complex patterns in nature is represented by so-called reaction-diffusion models, working by autocatalytic and counter-inhibitory mechanisms. Such mechanisms were first postulated by Alan Turing in the early fifties, and much extended by Alfred Gierer and Hans Meinhardt at the Max-Planck-Institue in Tübingen (by including inhibition with these models). These simulation models are based on the recognition that no absolute symmetry exists in nature. Originating from most minute asymmetries, autocatalytic (self-enhancing) processes will locally increase a deviation from symmetry. To not let the system overshoot at this particular site, long-ranging inhibitory mechanisms (the "inhibitor")

will constrain the action of the so-called “activator”, and thus stable patterns in space and time will develop. One of the amazing features of these models is that their simple mathematics is reductionistic, but the patterns generated - by varying only a few parameters - can be almost endless, able to represent highly individual forms and shapes as really found in nature (Meinhardt, 2009).

Epilogue on “Life – Individual – System”

Unnoticed, I have– with admittedly personal views – turned some conceptions of genetics from head to foot. As cells cannot be understood without considering their surrounding neighbours, genes remain ineffective without being regulated. What is at the origin of a new life, of a new individual? Is it merely genes, the new genome? No, certainly not. It is a distinct life situation, a certain (molecular) shape of the egg cell, into which the new genome now is “inferred”, and which is only set into action by a given (molecular) egg shape. Individuality does not momentarily emerge from the newly mixed genome of a fertilized egg, but is the product of a developmental process, which depends probably more on its *Umwelt* than on its genome (on defining *individuality of a person*, see Spaemann, 1996). “Life” could thus be conceived as a continuum from cell to cell, from organism to organism, from generation to generation, thereby experiencing (and interpreting) constant changes of environments. Genetic information represents an indispensable vehicle, a mere toolery, to sustain the ongoing of life, but is not an autotelic end purpose of nature by itself. Such a perception of “life” appears much in line with Meyer-Abich, when he speaks of “Mitsein”, or of “Mitwelt” (*being-with-the-world*), e.g. perceiving life as ever-lasting mutual interactions of the *Givings* and the *Takes* by all living beings in conjunction with non-living material things (Meyer-Abich, 2010). Under such premises, it remains an unconceivable riddle how some strict reductionists can reduce the phenomenon of “life” to a mere dissemination of egoistic genes (Dawkins, 1976). Relating the presented developmental concepts to evolution, I am convinced that back then - about 4.6 billions of years ago - similar principles held true: that it was the however conditioned environments (Umwelt) which shaped their “necessary genes”, but not inversely, that it should have been genes that multiplied and selected themselves egoistically to thereby produce –as an epiphenomenon - what we know as living nature.

Literature cited:

Alberts, B. et al. (2004). Molekularbiologie der Zelle, 4. Auflage, Wiley-VCH-Verlag, Weinheim.

Amundson, R. (2005). The changing role of the embryo in evolutionary thought. Cambridge Studies in Philosophy and Biology.

Arthur, W. (2011). Evolution. A developmental approach. Wiley-Blackwell.

Dawkins, R. (1976). Das egoistische Gen, RoRoRo Verlag (Aufl. 1996).

Gilbert, S.F. (2010). Developmental Biology, 9th Edition, Sinauer Ass., Sunderland USA.

Haeckel, E. (1998). Kunstformen der Natur (Nachdruck der Farbtafeln von 1904). Prestel-Verlag, München – New York.

Jahn, I. (Hrsg.) (2000). Geschichte der Biologie, 3. Auflage, Spektrum Akademischer Verlag Heidelberg, Berlin.

Layer PG (2007). Was ist Leben? - Von Zellen und anderen Lebewesen zwischen Genkonstanz und Umweltvarianz. In: Arnoldshainer Texte, Band 136 (Hrsg. H. Düringer, H. Meisinger, W.-R. Schmidt), Haag + Herchen Verlag, ISBN 978-3-89846-494-9, S. 102-116.

Layer, P.G., Araki, M. and Vogel-Höpker, A. (2010). New concepts for reconstruction of retinal and pigment epithelial tissues. Exp. Rev. Ophthalmol. 5(4), 523-544.

Meinhardt, H. (2009). The Algorithmic Beauty of Sea Shells (The virtual laboratory). Springer.

Meyer-Abich, K.M. (2010). Was es bedeutet, gesund zu sein. Philosophie der Medizin. Hanser-Verlag; (see dto. 1997: Praktische Naturphilosophie - Erinnerung an einen vergessenen Traum. C.H. Beck).

Nüsslein-Volhard, C. (2004). Wie Gene die Entwicklung steuern, C.H. Beck Verlag.

Spaemann, R. (1996). Personen. Versuche über den Unterschied zwischen „etwas“ und „jemand“. Klett-Cotta, Stuttgart.

Figures:

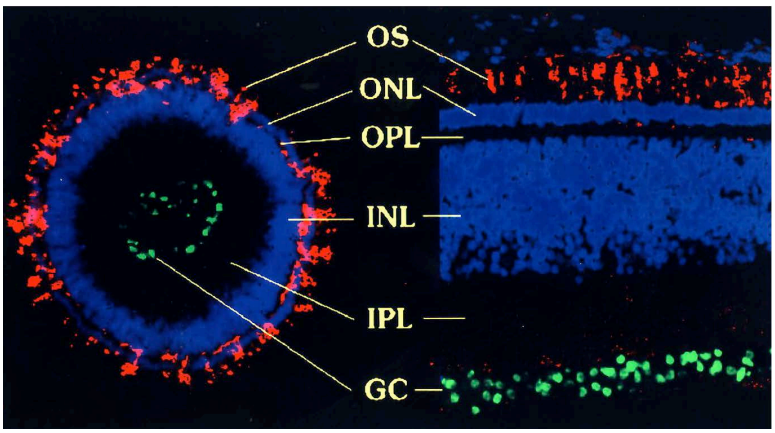

Fig. 1. Embryonic chicken retina (right) and retinal spheroid (left; see Layer et al., 2010). Nearly complete retinal tissue can be reconstructed from dissociated cells of a chick embryo. Note that in both structures the tissue consists of three nuclear layers (ONL, INL, GCL) and two synaptic "plexiform" layers (OPL, IPL), including all major retinal cell types (red, photoreceptors; green, ganglion cells).

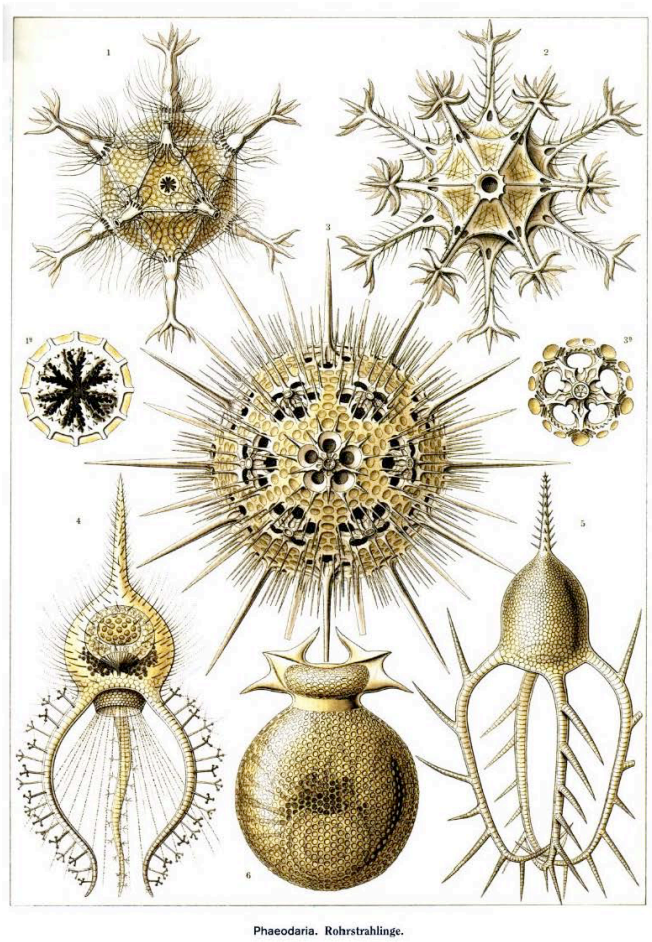

Fig. 2. A plate from Haeckel´s "Kunstformen der Natur" of 1899, showing various diatoms. Each one represents a unicellular organism (syst. "Protista"). Supposedly, Haeckel was fascinated by their

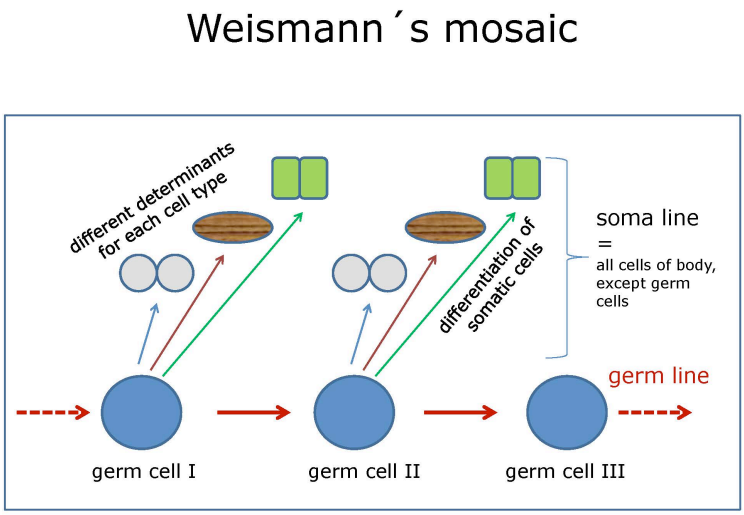

Fig. 3. Weismann´s idea about a fragmented use of *determinants* for the production of individual cell types of the body not only founded his hypothesis of *mosaic development*, but also was most influential on future conceptions of heredity. Accordingly, only germ cells would contain all determinants (later being called "genes"), which would be transferred from one generation into the next ("germ cell I", "germ cell II", etc.).

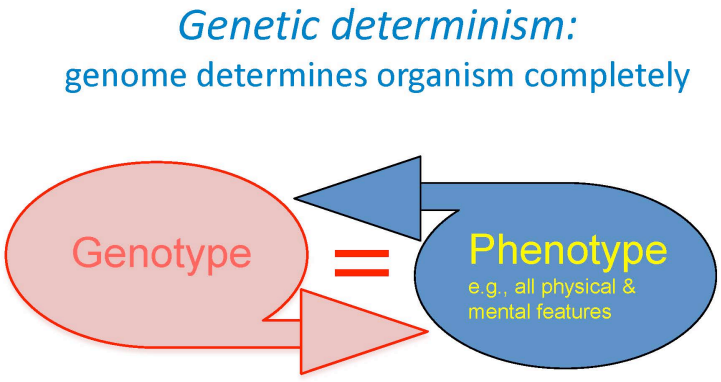

Fig. 4. The misconception of *genetic determinism* held that the genotype completely determines the phenotype. Thereby, environmental influences were neglected. Such ideas were particularly influential on promoting the evolutionary theory of population genetics.

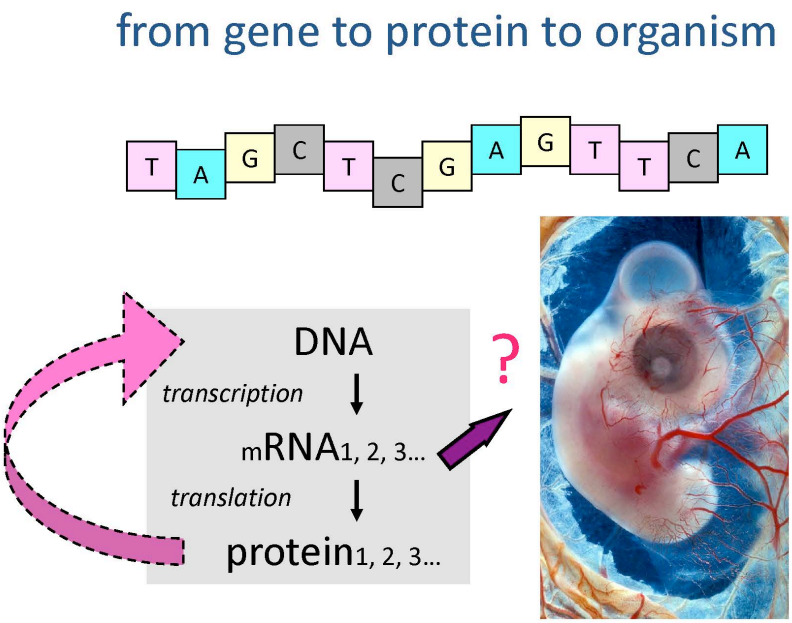

Fig. 5. A long way from genes via proteins to a living organism (6 day-old chicken embryo, right). Note that one gene can code for more than one messenger RNA, and for many more proteins. Importantly, during early embryonic development many proteins induce further "downstream" genes to be expressed (feedback mechanisms; arrow).

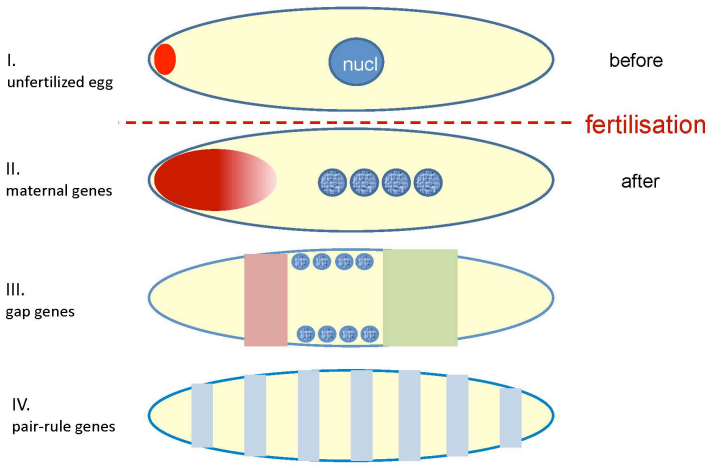

Fig. 6. Whether a fly will develop normally, depends already on the local distribution of particular gene products in the unfertilized egg ("maternal genes"; see red dot in I.). After fertilisation, this information is transferred into a graded distribution of the corresponding protein (II., red area in anterior part of egg); then, along with rapid nuclear divisions ("nucl", blue circles) a cascade of gene activations will initiate local subdivisions of the embryonic space into first irregular domains (III., "gap genes"), before segmentation by "pair-rule genes" sets in. Further see (Nüsslein-Volhard, 2004; Gilbert, 2010).