

EPISELECTIVE EVOLUTION

V.G.Cherdantsev, A.G.Kreslavsky, and A.S.Severtsov

Evolutionary Theory Department
 Faculty of Biology
 Moscow State University
 Vorob'evy gory
 Moscow 119899
 Russia

Received 25 February 1994, 11 November 1994

ABSTRACT: We consider the following group of evolutionary phenomena which we call episelective, insofar as they cannot be reduced to either direct or correlative effects of selection operating on fitness: (1) the appearance of new (or destruction of old) developmental correlations if expressed only in a reorganization of the phenotypic variation pattern, without a change in the phenotype itself; (2) the origination of morphological novelties on the basis of developmental self-organization; (3) the origination of new selective trends as a result of change in genic or non-genic mechanisms of phenotypic self-reproduction; (4) directional transformations of the phenotype on the basis of nonspecific and randomly directed effects of selection. At the heart of these episelective phenomena lies a structural complication (a lowering of the symmetry order) of developing systems, this leading to an increase in the number of processes being reproduced on the macroscopic scale and, consequently, to the origination of new evolutionary trends without respect to any change in specific trends of selection. The basic distinction between selective and episelective processes is that the former operate on an uncountably infinite number of fitness components, while the latter operate on a countable number of spatially ordered structures capable of self-reproduction.

*

*

*

By definition, fitness is the only phenotypic property subject to direct selection. Therefore, in the framework of the Modern Synthesis, phenotypic evolution is a set of correlative effects of selection operating on fitness (Wright, 1968-1969; Lewontin, 1974; Maynard Smith, 1982). There are three types of correlative effects that are usually considered. First, there is correlative selection of morphogenetic or functional components of the developing system, provided that each of these components makes a contribution to the fitness of the system as a whole. This is a well-known phenomenon and is called indirect, correlative, or associated selection, co-selection, and so forth. Second, the joint (coherent) evolution of characters may arise from the stability of morphogenetic mechanisms. This simply means that a pattern of morphogenetic interactions which has proved to be adaptive in the previous evolutionary history circumscribes the possible range of further phenotypic transformations (Gould and Lewontin, 1979). Third, due to pleiotropy and gene interactions, the correspondence between genes and fitness is also subject to selection, leading to a canalization of development (Waddington, 1940; Schmalhausen, 1946; Shishkin, 1984).

*

*

*

Evolutionary Theory 11:69-87 (January, 1996)

The editors thank B. Hallgrímsson, W. Scharloo, and another referee for help in evaluating this paper.

wild type. In particular, this is true for sternopleural bristles in *Drosophila*. The number and allocation of the macrochaetes is not subject

Thus, correlative effects arise as a result of the joint selection of initially independent components of the developing system or, alternatively, from their initial developmental connection. **In both cases it is selection that represents a rate-limiting (slowest) process in the formation of new (or destruction of old) correlations between these components.** If, however, the evolutionary transformations of a correlation pattern between the system components take less time than the change in phenotypic fitness of the system as a whole, then these transformations cannot be connected with selection in any causal way. The reason is simply that causal relationships between processes with different time scales are out of place. This paper aims to recognize and classify evolutionary transformations of this kind: by analogy with Waddington's epigenetic developmental processes (Waddington, 1940) it is natural to call them episelective evolutionary processes. There are at least four groups of phenomena which seem to lie beyond the scope of direct or correlative effects of selection.

1. Episelective structuring of variability

It is rather evident that Waddington's model of an "epigenetic landscape" (Waddington, 1940) can be related both to the general organization of developmental pathways, and to the organization of variability in adult phenotypes. Both in the course of development and in the adult state, directions and limits of continuous and structurally stable changes in phenotypic values of characters are circumscribed by the same morphogenetic constraints. It is trivial enough that new patterns (directions and limits) of adult variation cannot arise without a change in morphogenetic mechanisms. Less trivial is the question concerning the rates of morphogenetic evolution as compared to rates of selective changes.

From the Modern Synthesis point of view, developmental chreods arise as a result of stabilizing selection (Waddington, 1940; Schmalhausen, 1946). From this perspective, morphogenetic changes leading to a change in the adult (definitive) variation pattern must be associated with changes in fitness. This means that it is morphogenetic evolution that represents a rate-limiting component of the evolutionary process. In this (and only in this) sense variation of definitive phenotypes can be considered as something distinct from developmental variability.

We propose that the real course of morphogenetic evolution does not fit well into this generally assumed scheme. Recall that any developing system capable of self-regulation is **degenerate** in the sense that the same phenotype can be created by morphogenetic mechanisms which may differ from each other in many essential details but not in net adaptive value. Furthermore, morphogenetic mechanisms seem to evolve faster than the definitive forms (Filatov, 1939), so the choice of a mechanism may depend simply on contingencies of evolutionary history. Therefore, change in the variation pattern, which is in any case an inevitable consequence of morphogenetic evolution, may prove to be an **epiphenomenon** of the evolutionary process unrelated to any change in fitness. In such a case the separation between developmental and adult variation becomes purely conventional.

Thus, the constancy of proportions in a one-dimensional morphogenetic system (*Hydra* provides the simplest example) can be controlled in two different ways (for details see Belousov, 1987). There may be a morphogenetic mechanism providing a "scaling", i.e. an independence of proportions with respect to the absolute size of the system. If there is

no such mechanism, the constancy of proportions can be based only on constancy of absolute size. Consequently, in the first case we can observe a selectively neutral variation of size which will be absent in the second case.

The well-known difference between determinative (in most *Protostomia*) and non-determinative (in most *Deuterostomia*) modes of early cleavage can be treated in a similar way. In the first case each of the primary embryonic anlagen is a clone (or polyclone) descending from a definite blastomere (or blastomere group). In the second case the clonal organization of the embryo is absent, the reason being that all lineages are subject to individual variation: in different embryos the descendants of the same blastomere may even fall into different germ layers (Moody, 1987). In an obsolete view, determinative cleavage was believed to lead to the loss (or decrease) of regulative capacities at the early developmental stages. If this were the case, one could have considered non-determinative cleavage as more adaptive. However, modern data (reviewed by Bigellaar, 1982) show that all varieties of morphogenetic interactions known for the "regulative" type of development are manifested in determinative cleavage as well. The only difference is that regulation in determinative cleavage is based on interactions between single cells (blastomeres), while in non-determinative cleavage these interactions are manifested on a scale of cell groups. The larger such a group is, the less is the regulation of its cell number and cell lineages. Thus, the origination of a new mode of variation - variation of cell lineages - is shown to be an effect of morphogenetic evolution.

Note, however, that this effect implies a creation of new morphogenetically significant units: cells are replaced by embryonic tissues, as in the previous example. The old and new morphogenetic units are not homologous, simply because there is no room for homology between constant (determinative cleavage) and variable (non-determinative cleavage) elements. The lack of homology means that the continuity of developmental information carried by these elements is lost (Van Valen, 1982). However, this does not mean a loss of continuity in the developmental programme which forms the definitive phenotype, even if we assume that the substitution of morphogenetic units somehow affects phenotypic fitness. In any case, selection can discover that it deals with new morphogenetic units only after the substitution has occurred. In this sense we may say that, in the course of re-organization, mechanisms of phenotype formation evolve faster than the phenotype itself does, so that at **this** evolutionary stage the mechanism and the result of development cannot be matters of a correlative transformation.

Canalization

Similar episelective changes in morphogenetic mechanisms may occur even with small and continuous variation in the population means of metric characters, provided that we are considering a non-homogeneous spatially ordered structure. Thus, the canalization of variability may also be of episelective nature.

In those cases, in which canalization is a property which is inherent to the wild type, we can hardly reject (yet cannot prove) that this is due to stabilizing selection. The number and location of scutellar bristles in *Drosophila* provides one of the classic examples (Waddington, 1962). However, in many cases the canalized pattern does not coincide with the wild type. In particular, this is true for sternopleural bristles in *Drosophila*. The number and allocation of the macrochaetes is not subject

to variation. As for the microchaetes, they form a single row provided that their number is no more than six (for details see Kreslavsky and Dervis, 1987.) Thus, when the number of microchaetes is sufficiently small, their development depends on a prepatter. If, however, the number of microchaetes is more than six, the buffer capacity of the prepatter proves to be exhausted, so that the additional microchaetes arise outside of the initial row, with no spatial order on their own. There are two points that merit consideration: one is that variability in the number of microchaetes drastically increases when their number reaches a threshold value (which is equal to six), and the other is that the mean value of sternopleural microchaetes in wild populations of *Drosophila melanogaster* is above this threshold (Kreslavsky and Dervis, 1987). It follows that any kind of selection concerned with the number of sternopleural bristles passes through a point in which correlation between the number of bristles and the number of determined sites which they can fill is lost. At this point the mechanism of bristle positioning is subject to change (loss of a dependence on the prepatter), without a change in the phenotypic value of the selected character. In fact, the change in this mechanism is manifested only in the increase of phenotypic variability.

It is remarkable that the detailed analysis of scutellar bristles (Waddington, 1972) leads to the same conclusion. A canalization zone is characteristic not only of the wild type (four bristles situated in the corners of the scutellum), but also of any number of bristles which is a multiple of four. The reason is that, if the number of bristles is two, four or eight, bristles are situated at the defined points of the scutellum, distances between bristles tending to be equal. With any other (especially odd) number, the spatial distribution of bristles becomes disordered. Again, variation in the number of bristles leads to a threshold change in their positioning mechanism. As a result of its threshold nature, the connection between the mechanism of the phenotype formation and the phenotype itself (the number of bristles) cannot be liable to any kind of selection.

There is good reason to claim that any novel structuring of morphogenetic variation is episelective. In general, development can be portrayed as an alternation of variable and conservative (nodal) developmental stages. Variation at morphologically variable stages is degenerate, insofar as it vanishes (with no effect on further development) at the next nodal stage. However, taxonomic differences (especially those between higher taxa) arise at variable rather than at nodal developmental stages (Cherdantsev, 1993). We seem to have a classic example of Darwinian divergence - the individual variations are being converted into taxonomic differences. It is clear, however, that the Darwinian mechanism of divergence is not involved here, because of the degeneracy of the variation.

Neurulation

The evolution of neurulation in the anamniotic vertebrates provides a simple and carefully studied example (Filatov, 1939). From the purely morphogenetic point of view, the formation of the neural tube includes two processes: one is the aggregation of presumptive neuroectodermal cells on the dorsal side of the embryo, while the other is the formation of a cavity inside this aggregate (the neural-tube cavity). In *Amphioxus* and amphibians the aggregation of neuroectodermal cells causes a bending of the neuroectodermal cell layer, thus providing a mechanism for the formation of the neurocoel. In lampreys and teleosts cell aggregation proceeds without a bending of the cell layer, thus giving rise to a solid

cell mass. The neurocoel appears at a later stage, the cavity being formed by delamination inside this mass.

A simple experiment (Detlaf, 1938) shows that selectively controlled evolution can be excluded: when the outer cell layer is removed from the presumptive neural plate of an amphibian embryo, neurulation proceeds just as in teleosts. Therefore, selection for the change in the neurulation mechanism was precluded for at least two reasons. First, the difference between neurulation modes does not go beyond the scope of the initial (genetically determined) reaction norm of the neurulation process, and, second, the neurulation process is degenerate, insofar as different neurulation modes lead to the same morphological structure.

The difference between these modes is obviously connected with mechanical properties of the cell layer. The translocation of cells in a cell layer (in the aggregation process) will cause a bending of the layer as a whole, provided only that the active cell movements (which tend to decrease the surface area of the cell layer) produce a passive (elastic) reaction in neighbouring cells. This, in turn, is possible provided that the cell layer is sufficiently rigid. The increase in rigidity inevitably leads to a situation in which strains resulting from compression become, from the energetical point of view, less stable than strains resulting from bending. At that moment (i.e., with some threshold value of rigidity) the aggregation process becomes unstable in the sense that any random (indefinitely small) increase in the local cell concentration will produce a bending of the epithelial sheet.

It is known (see, for example, Belousov et al., 1975) that the mechanical rigidity of cell layers depends mainly on the rigidity of the outer surface of the embryo. In teleosts the outer surface is morphologically separated from the presumptive neuroectoderm, because the outer cell layer is converted into the extraembryonic envelope (periderm). Thus, rigidity of the neuroectodermal cell layer is decreased by the loss of its epithelial structure. In contrast, the amphibian neuroectoderm is one of the outer-layer derivatives, the rigidity of this layer being increased as a result of the thickening of the egg's cortical layer.

Just as in the previous examples, this leads **only** to the appearance of a new channel of variation in the neurulation process, with no effect either on its efficacy nor on its definitive result. It would be erroneous to consider this a correlative effect of selection operating on the egg cortex. In fact, after rigidity has reached a critical level, the change in the neurulation process can be caused by small random fluctuations. **At this stage** there is no correlation between the intensity of selection and the rate of morphological change.

Furthermore, these morphological changes are not related to the direction of selection. Adaptive specialization of the outer cell layer is a general and invariant trend in the evolution of early development. In anamniotic vertebrates this trend is most prominent in teleosts. The increase in rigidity of the outer egg surface in amphibians (especially in anurans) is a step in the same direction. Thus, from the selective point of view, amphibians occupy an intermediate position between teleosts and ancestral forms (*Amphioxus* and lampreys). However, at the episelective level, when we consider only morphological differences in the neurulation process, these taxa should be grouped in another way: amphibians should be united with *Amphioxus*, and teleosts with lampreys.

Other examples

The episelective structuring of variability may arise at fairly different taxonomic levels. In particular, it may be observed at the level of intraspecific differentiation. The common European leaf-beetle, *Gonioctena viminalis*, comprises two subspecies, *G. v. viminalis* and *G. v. rufus*. The colour pattern of the elytra is quite variable, the variation limits being coincident in each subspecies: from the complete elimination of dark spots, up to their complete confluence. The colour pattern is too variable to perform a recognition function. Therefore, this pattern *per se* is not connected with the divergence in any causal way, and this is confirmed by the fact that the limits of variation are not narrowed. However, the organization of this variation is quite different. In *G. v. viminalis* each dark spot enlarges isotropically, while in *G. v. rufus* there are preponderant directions in which the dark spots enlarge and fuse into larger spots. This seems to be connected with the difference in microsculpture of the elytra. The elytral microsculpture, however, has no adaptive value on its own (Kreslavsky, 1978). Therefore, the divergence in the variation patterns is not a correlative effect of selection, or whatever caused the change in microsculpture. The point is that on the **macroscopic** scale the effect of **microsculpture** is expressed only in the decrease (in *G. v. rufus*) in the number of ways in which the elytra may grow dark, while the typical (modal) colour patterns in both subspecies are indistinguishable. To recognize the difference, one needs to compare long colour-pattern series, and one can hardly assume that such a comparison may have a natural analog.

At the definitive (functional) developmental stages the degeneracy of the developing systems is manifested by the fact that the same function can be performed by distinct, although functionally equivalent, morphological structures. The evolution of the process of eversion of the tongue in amphibians (Severtsov, 1974) provides an example of episelective evolution at the functional level.

In all *Anura* the anterior margin of the tongue is fixed on the mandibular symphysis, the posterior margin lying freely in the mouth cavity. The contraction of muscles in the bottom of the mouth cavity lowers the mandibular symphysis thus drawing the tongue out of the mouth. In lower *Anura* (*Bombina*, *Pelobates*) the contraction of these muscles increases the pressure in the lymphatic canals in the tongue, leading to protrusion of the tongue. However, the tongue, when protruding, does not change its length.

In higher *Anura* (*Ranidae*, *Bufonidae*) the tongue acquires a layer of its own muscles (*m. genioglossus*). The contraction of these muscles pushes the lymphatic fluid into the free end of the tongue, leading to tongue elongation. To provide this mechanism, the originally separate lymphatic canals form a single lymphatic cavity. In addition, in higher anurans the length of the tongue in the ground state is greater than that in the ancestral taxa.

It follows that the intensification of function is a structured process consisting of at least two different components: one is the length of the tongue in the ground state, while the other is the additional elongation of the tongue in the extrusion process itself. The relative contributions of these components differ significantly with no difference in their overall efficacy (which is determined by the length of the extruded tongue). In toads the tongue in the ground state is shorter than it is in frogs, this being compensated for by a greater amount of tongue elongation during the process of extrusion.

In toads the tongue is of oval shape, the wide lymphatic cavity having short and wide diverticula. Thus the tongue shape does not differ significantly from that in the ancestral forms. In frogs, however, the free end of the tongue has two long lateral prongs flanking (in the ground state) the larynx, the diverticula of the lymphatic cavity being long and narrow.

The change in the tongue shape has no adaptive value in itself. At the same time, this is not a correlative effect of selection. In fact, the mechanism of tongue elongation is structurally degenerate in that the same overall functional effect is reached by **independent** changes in the components of the ancestral morphological construction. The only possible explanation is that the change in the tongue morphology results from a **new** morphogenetic correlation that arises between the shape and the length of the tongue. This means that in the ancestral group of frogs ancestral group the length of the tongue reached a threshold value beyond which a further tongue lengthening becomes morphogenetically dependent on the change in the tongue shape. As in the previous example, the appearance of a new morphogenetic correlation must have been initially expressed only in the canalization of variability. In fact, this correlation only restricts the number of ways in which the developing tongue could increase its length.

Inherent developmental variability

In all the examples given in this section, the appearance of new (or destruction of old) developmental correlations is expressed only in reorganization of the phenotypic variation pattern, without a change in the phenotype itself. Thus, besides the usual genetic and environmental components of variance, there is a component which may be called "inherent developmental variability": this refers to variation in quantitative morphological characters which results exclusively from destabilization of morphogenetic correlations in the process of their rebuilding. In mathematical terms, the connection between the changes in the phenotypic variation pattern and in the phenotype itself is identical to that between the dynamics of variables and of the parameters in common differential equations. As a result of the difference in the spatiotemporal scales, the variables may have only a threshold dependence on the parameters. It follows that their correlative change is meaningless.

Morphogenetic variation which emerges with a change in the mechanism of phenotypic development and does not correlate with the change in the phenotype itself, underlies all the other episelective phenomena.

2. The origination of morphological novelties

The formation of evolutionarily new morphological patterns, both in the course of development and in the adult state, can be understood only in connection with the episelective structuring of variability described in the previous section. Actually there is a deep, although not complete, analogy between the origination of evolutionary novelties and physical self-organization. In both cases the system should lower the order of the structural symmetry. This means that differences which arise between the initially indistinguishable parts of the system should be expressed directly at the macroscopic level, i.e. on a scale which is compatible with that of the system as a whole. Second, in both cases the new structuring emerges with small arbitrary fluctuations of the initial form. Finally, biological self-organization implies a condition which is of no

relevance to the physical systems: the structure that emerges in the self-organization process cannot perform any definite function. It is the last condition that makes it impossible for there to be selection for this kind of structure.

The mechanical catastrophe seem to provide the simplest way to initiate a new morphology on the basis of self-organization. Thus, from the mechanical point of view, many biological objects can be considered as actively growing elastic shells. Since the passive reaction to the active growth generates tensile stresses, the feedback between the passive and active strains is strongly non-linear (Belousov et al., 1975; Cherdantsev and Scobeyeva, 1994). Therefore, slow and continuous change in the shell geometry or microsculpture may lead the system to a bifurcation point in which the initial morphological state becomes unstable, this leading to the threshold origination of new geometric singularities. If, for example, in the initial state the shell represents an ellipsoid of revolution, then, provided that the shell is sufficiently rigid, and the difference in length between the long and short axes of the ellipsoid is sufficiently large, the increase in the intrinsic pressure generates longitudinal stretching and transverse compression of the shell. The initial mechanical equilibrium becomes unstable, and small random fluctuations of the initial form lead to the formation of longitudinal folds. This is a sufficiently realistic way in which the churn-staff structures typical of the vegetal outgrowth in plants (for example, in the unicellular alga *Acetabularia* (see Martynov, 1975, 1982) or colonial hydroids (Belousov, 1987) could have originated.

It would be improper to consider this kind of process as selective even provided that the bifurcation parameter is under selective control. Thus, in the case of *Acetabularia*, the bifurcation parameter is likely to be concerned with the rigidity of the cell wall. Before the appearance of folds in the outgrowing cell apex the rigidity cannot be changed except by a change in the thickness or microsculpture of the cell wall. In this case change in rigidity is a slower process than the outgrowth (swelling) of the cell apex under the turgour pressure. The appearance of folds drastically changes the situation. Since the fold size is of the order of magnitude of the apex as a whole, each fold can be considered as a rib of the growing apex. Thus, with complication of the form of the cell wall its rigidity increases at a rate which is identical to that of the outgrowth process. This is the reason why the complication of the form of the cell wall (in *Acetabularia* this corresponds to a formation of the umbrella) terminates its growth (Martynov, 1982).

The significance of this process is that the parameter becomes an additional variable, thus leading to an increase in the number of variables capable of direct interaction. Then, the reduction of symmetry order generates a new spatiotemporal scale, opening doors to a new morphogenetic process - in the case considered this is the interaction between the form and the rigidity of the growing cell wall. This also implies that there appear new variation channels, since the form, the number and the size of folds become matters of variation. However, in contrast to the examples considered in the previous section, these channels arise as a **consequence** of the phenotypic complication. As for the phenotype itself, its complication is a result of small random fluctuations of the initial form, which has lost its structural stability. Therefore, at the moment of origination of the new phenotype the heritability of this new variation is close to zero. This is not to say, however, that this variation cannot be adopted by selection at **later** evolutionary stages. In fact, in the case of *Acetabularia*, selection has

adopted a fluctuational difference between the "usual" (*A. mediterranea*) and "fringed" (*A. crenulata*) umbrellas (Martynov, 1982).

Episelective patterns in beetle elytra

In the leaf beetles of the subfamily *Cassidinae*, enlargement of the elytra is one of the common evolutionary trends. Because of developmental constraints this enlargement can affect only the elytral margins. Since the amount of material available for the enlargement is limited, there is produced a negative correlation between the thickness and the surface area of the elytra. Thus, in *Acromix spinifex* the elytra are perforated in many individuals. The origination of such perforations eliminates the initial morphogenetic correlation: the elytral surface area can be increased simply by an increase in the number or size of the perforations. Consequently, a new variation channel appears. This variation has no adaptive value on its own; however, it could have acquired it if the perforations were somehow used. For example, the male could have used them when mounting the female in copulation. In fact, in some genera of *Tenebrionidae* the analogous perforations on the margins of the first thoracic segment have become a taxonomically useful feature (Kreslavsky, 1978).

The pigment pattern of the leaf-beetle elytra arises in a similar way, and becomes one of the main adaptive features of a the taxon. Phylogenetically this pattern originates from the punctate distribution of the pigment (Kreslavsky, 1978). The pigment is concentrated primarily in the *columellae* (i.e., in the points of contact between the inner and outer surfaces of the elytra), and the morphogenetic reason is that the *columellae* correspond to the points which remain static in the course of elytral morphogenesis. Thus, in the ancestral state the pigment distribution is entirely subordinate to the elytral microsculpture, the latter being subject to random and adaptively neutral variation. Therefore, in the ancestral state the pigment distribution is not subject to selection.

On the other hand, since the connection between the pigment distribution and the elytral microsculpture is selectively neutral, there are no forces opposing independent selection of a general increase in the amount of pigment. If we assume that the pigment is accumulated in "untroubled" places (which are not subjects to strain during elytral morphogenesis), then we automatically get a positive feedback between the local concentration of pigment and the rate of its growth. In such a case, the initial connection between the pigment distribution and the elytral microsculpture will eventually be lost, being replaced by a direct interaction among the pigment spots. In fact, if the spots reach some threshold size, then they will fuse with neighbouring spots, and the spot distribution will acquire variation on its own which is independent from variation in the microsculpture. It is from this stage that a colour pattern gets the opportunity to acquire a function of its own, which may be cryptic or signalling. In both cases, the origination of a new function precedes selection, the latter participating only in the stabilization (or in the change) of the colour patterns that have already emerged at the macroscopic level.

Novelties in early development

Up to this point we have considered the origination of novelties at the definitive developmental stages. The same episelective mechanism works in the case when we are considering the origination of novelties in early

ontogenesis. The only difference is that in the latter case the novelties are of a higher taxonomic rank.

Thus, there is a general rule that the appearance of new embryonic tissues is associated with a complication of the embryonic spatial pattern. For example, in triploblastic *Metazoa* the formation of the third (mesodermal) germ layer is always associated with the acquisition of dorso-ventral polarity, which is absent in the ancestral state (in *Spongia* and *Coelenterata*). Therefore, the new embryonic tissue is not homologous to any of the pre-existing ones, this being a criterion of its novelty (cf. Van Valen, 1982).

In fact, the germ layers in diploblastic and triploblastic *Metazoa* are not homologous (Zakhvatkin, 1949). In diploblastic *Metazoa* the gastrula, from a topological point of view, corresponds to a sphere with a hole, the hole corresponding to the zone of presumptive entoblast and at which the cell sheet breaks down into single cells which emigrate inside the embryo. In triploblastic *Metazoa* the presumptive entoblast cells remain organized in a morphologically continuous epithelial sheet, and the emigration of single cells is replaced by epithelial invagination. Thus, the formation of the entoblast is not accompanied by any topological changes. The process of destruction of the epithelial sheet is preserved in the higher *Metazoa*, but the zone in which this process occurs is displaced to the circumference of the entoblast invagination. In all groups in which this process is not a result of a secondary transformation, the mesoderm is formed by the destruction of the cell epithelial sheet at the border between the ectoblast and the entoblast (see, for example, Beklemishev, 1964). It follows that the zone homologous to the zone of epithelial sheet destruction in the diploblastic *Metazoa* acquires a new shape (the shape of a ring) with a new topological dimension - the dimension of the torus.

Thus, a new germ layer (the mesoderm) appears as a result of the separation between the local (the destruction of the epithelial sheet) and non-local (the topological dimension of the destruction zone) characteristics of the ancestral embryonic tissue. At this evolutionary stage the connection between cell differentiation and morphogenesis is lost; consequently, the change in topological dimension cannot perform any definite morphogenetic function. The only effect of this change is the appearance of a new variation channel on the scale of the embryo as a whole. In fact, the torus, in contrast to the sphere with a hole, is something that **may** acquire a polarity which is distinct from that of the egg. In particular, any **local** fluctuation in the destruction process of the epithelial sheet will lead to the origination of a difference between the opposite sides of the circumference of the entoblast, which is a mark of dorso-ventral polarization. Thus, the correlation that arises between the mesoderm formation and the establishment of the **embryonic** dorso-ventral polarity is shown to be of episelective nature.

Novelties

The examples considered in this section show that the origination of novelties is based on the assimilation of new variation channels produced by the self-organization process. This is not to say, however, that the origination of novelties is identical to self-organization, i.e. to a mechanical or dynamical (Thom, 1969) catastrophe. The assimilation of new variation patterns is possible only if a new morphogenetic interaction appears in the system. This, in turn, implies an increase in the dimensionality of the space of dynamical variables that characterize the morphological diversity. Then, if the difference between the dynamical

variables and the parameters were not subject to change (as in the common models of developmental patterning), the episelective effects would have been extraneous. These effects are necessarily mediated by change in the spatiotemporal scales of morphogenetic processes: processes of a microscopic nature emerge on the macroscopic scale, or initially slow processes (or parameters) emerge on the time scale of the dynamical variables. This, and only this, provides a direct (continuous) integration between processes which were initially connected only in a threshold manner.

3. *The episelective origination of new selective trends*

In the previous sections we have examined situations in which phenotypic complication, or the reorganization of phenotypic variability, are not **primarily** connected with a change in fitness. In such cases **the further** evolution of morphological or morphogenetic novelties that have originated at the episelective level occurs by the usual selective process. However, fitness itself is also subject to episelective change. In this sense, and only in this sense, we can say that new trends of selection arise directly at the episelective level, without functional or environmental changes.

Episelective changes in fitness are always connected with important changes in the mechanisms of self-reproduction of the phenotype. The new self-reproduction mechanisms cannot originate in a selective manner, and the reason for this is quite evident. In fact, the notion of fitness can be unambiguously defined only if the population consists of phenotypes that use the same self-reproduction mechanisms. Imagine that the phenotypes use several modes of self-reproduction, and these modes differ only in that the choice of the mode influences the accuracy of self-reproduction. The phenotype which is "better" than the others only in accuracy of self-reproduction will force the other phenotypes out of the population, yet the Darwinian fitness of all the phenotypes in the population is equal. Therefore, the value of "the contribution to the next generation" will be of no relevance to the properties of the phenotype itself, i.e. to its fecundity, viability, and so forth.

Cilia of ciliates

Non-genic self-reproduction seems to originate on the basis of embryonic regulation. Thus, in ciliated *Protozoa* the somatic self-reproduction includes two processes: one is the non-genic reproduction of single organelles (cilia), and the other is the regeneration of missing macroscopic ciliary patterns at the cell scale (Frankel, 1984). This means that the basic properties of the developing systems responsible for embryonic regulation are included in the self-reproduction mechanism of the adult cell.

Thus, non-genic self-reproduction implies that the behaviour of microscopic elements must depend on their macroscopic environments. Since the scale of the elements is microscopic, relative to that of the macroscopic pattern which must be formed, the behaviour of neighbouring elements must be cooperative: each element should adjust its own behaviour with that of its neighbours. However, to prevent a spreading of the pattern throughout the whole cell, the cooperation must be short-range; therefore, there must be a long-range inhibition of the pattern-formation process. Recall that the combination of local activation with distant inhibition is a general cause of self-organization in reaction-diffusion

systems (Turing, 1952). Thus, there is a basic similarity between the systems capable of non-genic self-reproduction and the systems capable of self-organization.

Since the distant inhibition field has a finite size, any kind of selection in any way concerned with increase of cell size will inevitably lead to a threshold duplication of structures that possess a non-genic mechanism of self-reproduction. The same will come about with random fluctuations of cell size, or with environmentally induced changes in it.

Moreover, the recruitment of the duplication mechanism into phenotypic self-reproduction implies the origination of a new trend of selection. Thus, in ciliated *Protozoa* the danger from selfish reproduction of cilia must have initiated the selection for mechanisms that could have controlled this reproduction on the cell scale (cf. Buss, 1987). The formation of macroscopic gradients of "positional information" (Wolpert, 1969) is one of the possible decisions.

Origin of dominance

In all cases in which a system consists of self-reproducible elements which differ in the accuracy of their self-reproduction, the system as a whole may become subject to episelective evolution. The common diploid model responsible for the genetic reproduction of quantitative phenotypic characters provides an example.

Assume that the contributions of genes to the phenotypic value of characters fluctuate at random. This leads to the well-known phenomenon of directional dominance (Falconer, 1981), which in our case means the dominance of genes being in two opposite directions: in other words, both dominant and recessive alleles exert both (+) and (-) effects on the phenotypic value. As in the case of Muller's ratchet, the contribution of a dominant allele to the phenotypic value of a character will be reproduced with a greater accuracy than that of a recessive allele. Then, if the first cycle of selection tends to increase the phenotypic value, the frequency of dominant alleles with a (+) effect will exceed the frequency of recessive alleles with a (+) effect. If, in the next cycle of selection, there is a tendency to decrease the phenotypic value, then dominant alleles with a (-) effect will be preponderantly selected. Thus, the difference in the reproduction accuracy will lead to the directional fixation of wild-type dominance without respect to the direction of selection. In other words, if the optimal value of the character is subject to fluctuation, then the dominant alleles will be automatically accumulated in the wild type (for the details see Kreslavsky, 1987). This seems to solve the problem of the origination of dominance. It is known that the attempts at selective explanation are not satisfactory in this case (Wright, 1969).

Group effects

Up to this point we have considered self-reproduction at only the individual and intra-individual levels. However, phenotypic reproducibility of quantitative characters (i.e., in terms of quantitative genetics, reproducibility of their phenotypic values from one generation to another) may be necessarily connected with reproducibility of environmental conditions. This may be true for all plastic features of the individual phenotype, and for any supra-individual interactions.

In particular, when we consider the variability of any plastic phenotypic feature under natural conditions, the limits of actual variation are circumscribed not by the genotypic potential of individuals,

but rather by the range of specific environments in which the individuals usually develop. A deterioration of environmental conditions narrows the range of appropriate environments, and this may be accompanied by a shift in the mean phenotypic values of characters with respect to their optimal values. This is equivalent to a change in the environmental aspect of phenotype self-reproduction. The point is that the time for this change is shorter than that for genetic changes, thus leading to the episelective origination of new selective trends.

In fact, it is well known that an increase in the density of *Drosophila* populations leads to a decrease in body size, this being of purely environmental nature. The small flies are characterized by a decrease in fecundity, viability and longevity, and by an increase in their resistance to environmental stresses. All these changes proceed on the foundation of a pre-existing genetic correlation between the components of fitness and body size. Thus, the environmental alteration is the only cause of these changes. It is quite clear that in succeeding generations the unfavourable effect of the population density must be compensated for by selection. What is less clear, however, is the direction of selection and the way in which compensation will be achieved. One could expect that selection would tend to restore the initial values of the main components of fitness, with a corresponding increase in body size. However, this does not in fact occur (Kreslavsky and Dervis, 1987). Selection operates on other fitness components, primarily on the sensitivity of larvae to density, while the adult body size shows no regression toward the wild type. The reason is simply that *Drosophila* has no genes which in the magnitude of their effect on quantitative characters could compete with the effect of the drastic environmental deterioration. Thus, since the change in environmental conditions affects the phenotypic reproduction of quantitative characters, this leads to a revaluation of their contributions to fitness, leading to a new direction of selection.

All that has been said about the relationship between the diversity of environmental conditions and phenotypic plasticity may be applied to the relationship between group and individual behaviour. It is well known that group behaviour is less plastic than is individual behaviour. This is a case in which individuals construct their environments, thus limiting their own behaviour. If individual behaviour occasionally goes beyond the limits of the group norm, then, provided that learning or other forms of social inheritance are available, this also may initiate new selective trends.

Observations on the origination of predation by the seagull *Larus argentatus* provide an example (Busun, 1989). Reports of seagulls attacking other birds and small mammals appeared in the Russian literature about twenty years ago. Predation arises from the basis of the pre-existing habit of consuming corpses, i.e. as initially a result of opportunism in feeding behaviour. Seagulls start by devouring corpses of their dead nestlings, and then they begin to cannibalize their living young. In winter seagulls now set out to hunt birds of other species (for example, *Fulica atra*.) During the very short period in which they have had experience of predation they have learnt the methods of killing their prey and the methods of cooperation when hunting.

Young seagulls adopt these devices by imitating the behaviour of their parents or other adult birds. Selection can be initiated only after predation has become a group norm. Moreover, the change in individual behaviour is no more than a nongenetic modification of the phenotype, and its transmission to later generations is based on social inheritance.

Therefore, the new behavioral features may not be subject to selection. On the other hand, there appears to be an opportunity for selection for morphological adaptation to these features: for example, there may arise selection for change in the beak shape. The behaviour in this case is responsible only for reproducibility of a new selective requirement.

4. Directional transformation of the phenotype without directional selection

The non-reducibility of this phenomenon to direct or correlated effects of selection is immediately evident. What is a matter of difficulty is to pick out real examples. The reason is that all the examples seem to lie in the new (not only for biology) and scarcely studied field of morphogenetic self-organization.

The experimental study of artificial selection reveals an "asymmetry of selection response" (Falconer, 1981), which means that the response of the same quantitative characters to selection in opposite directions is not symmetric. In mice, for example, one response to selection for increase in litter size is expressed in an increase in ovulation rate. Selection in the opposite direction leads, not to a decrease in the ovulation rate, but to an increase in embryonic mortality (Falconer, 1960). Then, even if the direction of selection fluctuates at random, the morphogenetic systems involved in determination of litter size will be subject to directional change.

In most cases, however, the episelective directional changes in morphogenetic systems seem not to involve cyclic selection. Episelective drift is most likely to originate from the directional accumulation of non-specific and randomly directed effects of selection. This drift, if it really exists, cannot in any way be considered as a correlative effect of selection. Selection in this case gives the same effect as do random fluctuations.

In the evolution of morphogenetic mechanisms there is a large field in which directional evolutionary transformations do not imply any definite direction of selection. Thus, in morphogenetic evolution there is an absolutely universal trend of "developmental embryonization". From the strictly phenomenological point of view, "embryonization" means that structural and morphogenetic patterns of the developing system are subject to an evolutionary drifting from later developmental stages to earlier ones. The term is not successful in that it suggests associations with purely selective processes - the accumulation of yolk in the egg, maternal care of the embryo, and so forth (see, for example, de Beer, 1951.) In fact, however, the complication of embryonic structure by adopting the structural organization of later developmental stages may not correlate with any change in the ecology of early development. The evolution of the embryonic axial pattern in anamniotic vertebrates provides an example.

Evolution of vertebrate axial patterning

As this topic is too extensive (for details see Cherdantsev, 1991, 1993; Cherdantsev and Scobeyeva, 1994), we consider only the evolution of Spemann's primary embryonic induction. Recall that in evolutionarily derived forms Spemann's induction provides a connection between the anteroposterior differentiation of the axial mesoderm and the primary differentiation of the neural embryonic structures (see Spemann, 1936). In order to provide this, induction should meet at least two conditions. First, the inductive signal issuing from the presumptive axial mesoderm must be regionally specific. Second, the axial mesoderm must have regional specification of its own, which means regionalization pre-existing in the

tissue and being stable. Moreover, in the ancestral state neither of the two conditions is fulfilled.

Thus, in *Amphioxus* the inductive activity of the axial mesoderm is fairly devoid of any regional specification. Such nonspecificity could have been caused by the observed lack of neural anteroposterior differentiation. In lampreys, however, in which neural anteroposterior differentiation is quite distinct, the state of the inductive process is close to that in *Amphioxus*. Any fragment of the presumptive axial mesoderm, whatever its normal definitive anteroposterior position, may, in transplantation experiments, induce the formation of neural derivatives both of the head and of the trunk types. The choice between the two is a matter of the position which the transplanted material has happened to occupy in the host embryo. Therefore, the regional specification of the inductive process is not determined by initial regionalization of the presumptive axial mesoderm. At later developmental stages the inductive activity of the axial mesoderm does become determined by the regional specificity of the mesoderm itself. However, this comes about too late, when the regional differentiation of the neural structures is almost completed. Only in amphibians does the mesodermal anteroposterior regionalization become a property of the mesoderm itself at sufficiently early developmental stages. It is only from this stage of evolution that Spemann's induction can actually participate in the normal anteroposterior differentiation of the embryonic neural structures.

Thus, in the ancestral state (*Amphioxus* and lamprey) anteroposterior differentiation of the embryonic axial pattern is associated with self-organization of the presumptive axial mesoderm. This simply means that the process does not require any pre-existing regionalization of the mesoderm at the cell level, anteroposterior differentiation emerging immediately on the supracellular scale (for the specific model of this process see Cherdantsev and Scobeyeva, 1994.) As regionalization of the inductive signal primarily originates **after** the completion of anteroposterior differentiation, at this evolutionary stage induction cannot participate in the normal anteroposterior differentiation of the embryo. Therefore, selection for the origination of Spemann's induction is impossible. The only way in which induction could have acquired its morphogenetic function on its own is by embryonization.

In fact, in the ancestral state the capacity for regionally specific induction is only a **consequence** of the morphological anteroposterior differentiation. This means that the inductive capacity is primarily a property of the relatively mature (differentiated) cells. In further evolution the properties of mature cells are progressively shifted to earlier stages of the supracellular pattern formation. Then, these properties acquire a function as inductive signals, thus becoming a **cause** (certainly not the only cause) of anteroposterior differentiation. The morphogenetic interactions on the macroscopic scale are replaced by interactions at the molecular level.

Thus, we can construct the following evolutionary sequence. At the beginning the spatial pattern emerges immediately at the macroscopic level from an initially homogeneous system consisting of equipotential elements. The forms in which the origination of the same pattern is underlain by a prepattern are at the end of this series. The prepattern is defined on a smaller scale, i.e. on the scale of the system elements. This means that differentiation of the elements precedes the origination of the macroscopic spatial pattern. Therefore, we may see that in its evolutionary course the system progressively retreats from the real

self-organization threshold (the point at which the spatial pattern spontaneously emerges from the initially homogeneous system). Thus, in ontogeny the prepatter is a cause of the pattern, but the converse is true on the evolutionary scale.

This general scheme is confirmed by data concerning expression of the *Hox* homoeotic genes. The *Hox* genes expressed in the anterior region are situated on the 3' end of the chromosome fragment, indicating that these genes are derivatives (resulting from duplication) of the ancestral gene whose expression controlled the development of trunk structures. Moreover, the 3' genes are expressed at **earlier** developmental stages than are their 5' homologues.

Thus, the directional transformation of the developmental mechanism – the formation of prepatterns on the basis of the evolutionarily earlier pattern – does not require any directional selection. As the initial pattern emerges from a spatially homogeneous system in close proximity to the self-organization threshold, any occasional spatial heterogeneity at the earlier developmental stage will determine a time for the pattern emergence and a position of the boundary separating the pattern counterparts. Any kind of selection affecting this earlier developmental stage in an arbitrary way will lead to the establishment of a **causal** connection between the pattern itself and the structural organization of the preceding developmental stage. In addition, evolutionary movement in the opposite direction, which would make the system return to the self-organization threshold, is impossible. The reason is that the initial movement (away from the threshold) could be realized provided that it does not affect fitness. Consequently, direct selection for the reversal of this drift is also unfeasible. On the other hand, the accumulation of correlative effects of selection cannot lead to the restoration of a structural symmetry that was once lost.

The nature of episelective evolution: Structures vs. characters.

At the heart of the distinction between selective and the episelective evolution lies the basic distinction between characters and structures. Characters as Cartesian entities characterize not the system structure, but rather the interactions between the system elements, or between the system and its environment. It follows that the number of characters in any living system is uncountably infinite and, consequently, variation in almost all such characters is of no relevance to Darwinian fitness. On the other hand, the set of structures capable of performing adaptive functions is countable, if not finite. The reason is that any biological structure must have developmental mechanism of its own. A change in characters can generate a new structure only if the system lowers its symmetry order as a result of self-organization. In the simplest case this means that characters which in the initial state could be actualized everywhere in the system, become restricted to only a part of this system. This is the only way in which a part of the system – **but not the characters of this part** – becomes a new structural element. In principle this is equivalent to the origination of a new structural domain, which means that morphogenetic interactions emerge on a new macroscopic scale. It is the domain structure that makes the developing system degenerate. Indeed, the developing system becomes susceptible to those (and only those) changes that lead to a shift of a domain-separation boundary.

All the basic assumptions of the Modern Synthesis are true for characters, but this is not the case for structures. In fact, if there is

no structuring in the sense outlined above, then one may assume there is an uncountably infinite set of fitness components, any change in each of the components being dependent on an uncountable number of phenotypic features. This does not mean, of course, that the Modern Synthesis ignores organizational constraints. However, the constraints are presumed to be external in the sense that they are matters of correlative effects of selection (cf. Gould and Lewontin, 1979).

In contrast to structures, fitness components and all biological functions are the characters that adopt or reject all changes in developmental or ecological interactions. Therefore, there is no reason to attribute to structures any definite contribution to fitness. In principle, there is always the possibility of a continuous transition from any particular set of values of fitness components to any other set, while for structures this must be associated with a threshold change. Structural transformation, however, is reducible neither to a threshold effect of selection, nor to an effect of a common dynamical catastrophe. The reason is that the evolutionary significance of this transformation lies **only** in the emergence of new spatiotemporal scales of the morphogenetic processes. The slow parameters of a system begin to vary on the same spatiotemporal scales that the dynamical variables do, and this is a principal way of generating new variation patterns.

We may assume that the process of self-reproduction is a basic (very slow) parameter of the evolving living system. In fact, selective evolution begins with optimization of the self-reproduction process, so that in the course of further evolution we presume this process to be constant with respect to changes in fitness. It follows that self-reproduction has no additive genetic variance on its own. Thus, variation in the self-reproduction mechanism can originate only episelectively.

The episelective emergence of this variation has at least two principal consequences. First, it leads to the origination of self-reproduction at the intra-individual (mobile genetic elements and so forth) and at the supra-individual (social inheritance) levels. Therefore, the initiation of both intra-individual and supra-individual self-reproduction is possible only to the extent that these new modes of self-reproduction do not affect individual fitness at the time of their origination (cf. Van Valen, 1987).

Second, new structural domains (in contrast to characters) arise only at the episelective level. We have shown that the lowering of symmetry order in self-reproducing systems generates new mechanisms of developmental reproduction. This simply means an increase in the number of processes that are reproducible on the macroscopic scale. On the other hand, the lowering of symmetry immediately increases the number of ways in which the system can achieve the same adaptive result. Thus, an increase in the complexity of the structural pattern generates in the developing system new evolutionary trends which persist irrespective of any change in specific directions of selection.

Thus, episelective evolution is a result of any increase in **structural** complexity, provided that the latter comes from developmental self-organization. Since all evolutionary transformations that imply changes not in the characters but in the structure of the evolving system, are not subject to direct selection, all evolutionarily significant changes are of an episelective nature.

Literature cited

- Belousov, L.V. 1987. *Biologicheskii Morfogenez*. Moscow: Nauka. 237 pp.
- Belousov, L.V., Dorfman, J.G., and Cherdantsev, V.G. 1975. Mechanical stresses and morphological patterns in amphibian embryos. *Journal of Embryology and Experimental Morphology* 34: 559-574.
- Buss, L. 1987. *The Evolution of Individuality*. Princeton Univ. Press. 320 pp.
- Busun, V.A. 1989. Nekrofagiya, kishchnichestvo, kleptoparazitizm: razvitiye i vzaimosvyas' troficheskikh strategii u serebristoi chaiki (*Larus argentatus*). *Zoologicheskii Zhurnal* 68: 89-99.
- Beklemishev, V.N. 1964. *Osnovy Sravnitel'noi Anatomii Bespozvonochnykh*. 3rd Edition. Volume 1: Promorfologiya. Moscow: Nauka. 430 pp. [English translation, 1969: *Principles of Comparative Anatomy of Invertebrates*. Volume 1. Promorphology. Edinburgh: Oliver & Boyd.]
- de Beer, G. 1951. *Embryos and Ancestors*. Oxford: Clarendon Press. 160 pp.
- Cherdantsev V.G. 1991. Induktsiya i differentsirovka osevykh struktur u minogi: K voprossu ob evolyutsii pervichnoi embrional'noi induktsii. *Zhurnal Obshchei Biologii* 51: 89-103.
- Cherdantsev, V.G. 1993. Evolyutsionnaya samoorganisatsiya morfogeneza. In: *Sovremenniy Problemy Teorii Evolyutsii* [collective work], pp. 110-127. Moscow: Nauka.
- Cherdantsev, V.G., and Skobeyeva, V.A. 1994. The morphological basis of self-organization: Developmental and evolutionary aspects. *Rivista di Biologia (Biological Forum)* 87: 57-85.
- Detlaf, T.A. 1938. Neurulatsiya u beskhovostykh amfibii kak kompleksnii formoobrasovatel'nii protsess. *Trudy Instituta Eksperimental'nogo Morfogeneza Moskovskogo Universiteta* 6: 187-201.
- Falconer D.S. 1960. Genetics of litter size in mice. *Journal of Comparative Physiology* 56 (Supplement), pp.153-167.
- Falconer D.S. 1981. *Introduction to Quantitative Genetics*. London: Longman. 340 pp.
- Filatov, D.P. 1939. Sravnitel'no-morfologicheskoe Napravlenie v Mekhanike Razvitiya, Ego Ob'ekt, Tseli i Puti. Moscow: Nauka. 127 pp.
- Frankel, J. 1984. Pattern formation in ciliated Protozoa. In: *Pattern Formation. A Primer in Developmental Biology* (G.M. Malacinski and S.V. Bryant, ed.), pp. 163-196. New York: Macmillan.
- Gould, S.J., and Lewontin, R.C. 1979. The spandrels of San Marco and the Panglossian paradigm: a critique of the adaptationist programme. *Proceedings of the Royal Society of London (B)* 205:581-598.
- Kreslavsky, A.G. 1978. Nekotorie zakonomernosti izmenchivosti i evoyutsii risunkov na nadkryl'yakh zhukov-listoedov. Dissertation for the degree of Kandidat, Moskovskogo Gosudarstvennyi Universitet. Privately published.
- Kreslavsky, A.G. 1987. Otbor po strukturirovannim priznakam i napravlenaya evolyutsiya. *Zhurnal Obshchei Biologii* 49: 243-250.
- Kreslavsky, A.G., and Dervis, N.V. 1987. Ecologicheskie osnovy podderzhaniya izmenchivosti po chislu sternopleural'nykh shchetinok v populyatsiyakh *Drosophila melanogaster*. *Zoologicheskii Zhurnal* 66: 724-734.
- Lewontin, R.C. 1974. *The Genetic Basis of Evolutionary Change*. New York: Columbia Univ. Press. 280 pp.
- Martynov, L.A. 1975. A morphogenetic mechanism involving instability of initial form. *Journal of Theoretical Biology* 54: 471-480.

- Martynov L.A. 1982. Rol' macroscopicheskikh prozessov v formoobrasovanii. In: Matematicheskaya Biologiya Razvitiya [collective work], pp. 135-155. Moscow: Nauka.
- Maynard Smith, J. 1982. Evolution and the Theory of Games. Cambridge Univ. Press. 230 pp.
- Moody, S.A. 1987. Fates of the blastomeres of the 32-cell stage *Xenopus* embryo. Developmental Biology 122: 300-319.
- Severtsov, A.S. 1974. Evolyutsiya mekhanizmov zakhvatyvaniya pishchi i dykhaniya amfibii. Dissertation for the degree of Doktor, Moskovskogo Gosudarstvennyi Universitet. Privately published.
- Shishkin, M.A. 1984. Individual'noe razvitie i estestvennii otbor. Ontogenez 15: 115-136.
- Schmalhausen [=Shmal'gauzen, etc.], I.I. 1947. Factory Evolyutsii. Moscow: Nauka. 160 pp. (English edition, 1949: Factors of Evolution: The Theory of Stabilizing Selection. Philadelphia: Blakiston. Reprinted 1986, Univ. Chicago Press.)
- Spemann H. 1936. Experimentelle Beiträge zu einer Theorie der Entwicklung. Jena: Gustav Fisher Verlag. 190 pp.
- Thom, R. 1972. Stabilité Structurale et Morphogénèse. Paris: Ediscience. (English translation, 1975: Structural Stability and Morphogenesis. Reading, Massachusetts: W.A. Benjamin). 270 pp.
- Turing, A. 1952. The chemical basis of morphogenesis. Philosophical Transactions of the Royal Society of London (B) 237: 37-72.
- Van Valen, L.M. 1982. Homology and causes. Journal of Morphology 173: 305-312.
- Van Valen, L.M. 1987. Non-Weismannian evolution. Evolutionary Theory 8: 101-107.
- Waddington, C.H. 1940. Organisers and Genes. Cambridge Univ. Press. 223 pp.
- Waddington, C.H. 1962. New Patterns in Genetics and Development. New York: Columbia Univ. Press. 260 pp.
- Waddington, C.H. 1972. Form and information. In.: Towards a Theoretical Biology (C.H. Waddington, ed.), Volume 4, pp. 109-141. Edinburgh Univ. Press.
- Wolpert, L. 1969. Positional information and spatial pattern of cellular differentiation. Journal of Theoretical Biology 25: 76-89.
- Wright, S. 1969. Evolution and the Genetics of Populations. Volume 2: The Theory of Gene Frequencies. Univ. Chicago Press. 450 pp.
- Zakhvatkin, A.A. 1949. Sravnitel'naya Embriologiya Nizshykh Bespozvonochnykh. Moscow: Nauka. 211 pp.

