# THE WITHIN-INDIVIDUAL BASIS OF BETWEEN-INDIVIDUAL DIFFERENCES

**V.G. Cherdantsev, V.A. Scobeyeva**

Department of Biological Evolution, Faculty of Biology, Moscow State University, Moscow, Russia,
e-mail: VGCherdantsev@yandex.ru; skobei-khanum@yandex.ru

From the analysis of quantitative morphological dynamics of amphibian gastrulation, we infer a general law that, in the developmental series of repeatable embryonic areas subject to shaping, the proportion of within- to between-individual variation in different areas depends primarily only on a spatiotemporal order of their formation. The younger («distal») areas are more variable and develop at higher rates than the older («proximal») ones. Despite the absence of a notion of fitness, the general principle of morphogenetic dynamics is mathematically the same as that of selection, since the system tends to minimization of within-individual variance at a rate proportional to its amount. Thus, the within-individual component of variation seems to provide a driving force of morphogenesis, which means that the concept of developmental canalization is a bias.

**Key words:** variability, morphogenesis, repeatability, selection.

## Introduction

When in a sample of the adult organisms the amount of variance in metric characters expressed in the values of the coefficients of variation (*CV*) is about 20 % and more the biologist would suspect that something is wrong with sampling. Meanwhile, when we consider the embryonic structures, the values of the CV at a level of 15–20 % correspond not to the upper, but rather to the lower limit of variation in morphological characters that are subject to change in the course of normal development (Cherdantsev, Scobeyeva, 1994; Scobeyeva, Cherdantsev, 1999; Cherdantsev, 2003; Scobeyeva, 2006). Thus, the *CV* values of egg sizes in a single clutch of the common frog (*Rana temporaria*) spawn in nature never exceed 6–7 %. In the beginning of gastrulation, the yolk plug diameter varies in the same clutch at a 15–18 % level while characteristics of the dorsal blastopore lip shape vary in a range from 27 to 67 % (Cherdantsev, Scobeyeva, 1996; Cherdantsev, 2003). Variation of this order of magnitude is common to genetically homogeneous groups of embryos (siblings) developing in optimal environmental conditions and having the same developmental age (Scobeyeva, 2006). It follows that the normal developmental variation can be referred neither to genetic nor environmental components of variance. It merits being considered as a special developmental component of natural phenotypic variance – as the inherent developmental variability (IDV, see Cherdantsev *et al*., 1996).

There is a principal difference between the IDV and so-called «intangible» developmental variation (Falconer, 1981). The last refers to «accidents» or «errors» of development and, consequently, should increase with time. In contrast to that, the IDV is subject to increase with initiating of each new morphogenetic shaping of the embryo and decreases, as the developing structure acquires its eventual shape. This holds both for the shaping itself, such as the dorsal blastopore lip shaping in amphibian embryos (Cherdantsev, Scobeyeva, 1994; Cherdantsev, 2003; Scobeyeva, 2006), and positioning of gene expression domain boundaries, such as those between anteroposterior segments of Drosophila embryos (Houchmandzadeh *et al*., 2002; Jaeger *et al*., 2004). In both cases, instead of interfering with developmental pathways, the IDV seems to drive them, selecting and differentially enhancing the «appropriate» fluctuations, which suggests that identification of the IDV dynamics

with Waddington's canalization (Waddington, 1940) is not a matter of fact.

The nature of IDV seems to be the same as that of within-individual differences between the repetitively (serially) homologous structures of the adult organism. The repetitive homology means that a given series of structures, irrespective of the degree of their morphological divergence, arise with modification of parameters of the same developmental (parametric) program (van Valen, 1982). By definition, if more than one measurement of a morphological character can be made in each individual in space and time, the phenotypic variance can be partitioned into variance within individuals and variance between individuals (Falconer, 1981).

One of the basic principles of morphogenesis is that of spatial unfolding stating that the shape differences of embryonic areas display the succession of shaping of the same area (Cherdantsev, 2003, 2006). Therefore, a measurement made in the structure can be partitioned into components corresponding to the consecutive stages of its shaping. This is sufficient for considering the developing structure subject to shaping as an analogue of repetitively homologous structures, which provides an opportunity of partitioning of their variance into the between- and within-individual components.

Our aim here is to show that lying at the heart of the IDV is the within-individual variation. The point is simply that, if the differences between repetitively homologous parts form a one-parametric set whose elements are at consecutive stages of the same developmental transformation, then their own variances are added by positive covariation being proportional to the degree of within-individual spatial differences. The between-individual variance increases at the expense of the within-individual one, that is, at the expense of spatial heterogeneity of the developing structures in each given individual. This explains why variation in quantitative characters connected with embryonic shaping proves not a hindrance, but rather an impetus of their directional change. We will purpose to show that in the developing structure consisting of repetitively homologous elements each element moves towards minimization of within-individual variance of the whole structure at a rate proportional to the amount of variance.

## Spatiotemporal repeatability in amphibian gastrulation and its implications

**Analysis of variance in synchronously developing embryos fixed at consecutive stages of morphogenesis.** The hierarchical commitment inherent to determination of embryonic rudiments is a particular case of the spatiotemporal series of repeatable serially homological structures. In amphibian gastrulation this series begins with outlining of the blastopore circumference, the so-called marginal zone (MZ), whose inner diameter (*Lyp*, see Fig. 1, a) is the only metric character that can be measured at the vegetal view of the whole gastrula prior to the appearance of the dorsal blastopore lip (DBL). The further succession of morphological events develops as a series of local shaping of the blastopore circumference initiating at the dorsal pole of the MZ and traveling to the ventral pole (Figs. 1, b–d).

The DBL appears as a cleft whose orientation is that of the tangent to the blastopore circumference (Fig. 1, b). It follows that at this stage the DBL has no planar curvature on its own and the only measurements characterizing the shape of DBL are that

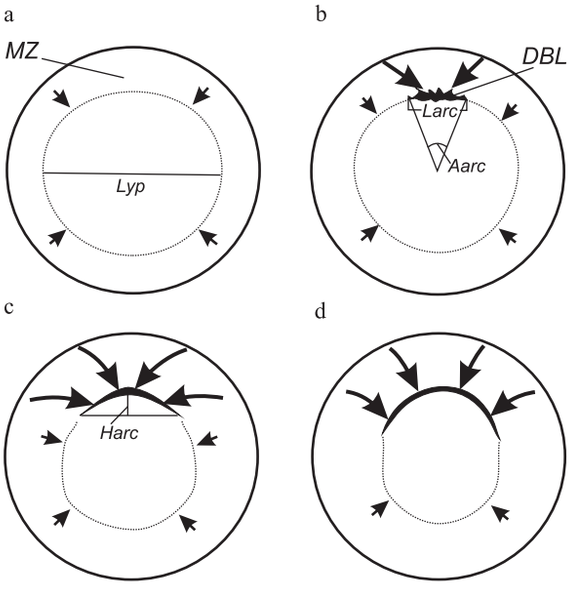


**Fig. 1.** Spatiotemporal repeatability of morphogenesis in frog gastrulation.

a – blastopore circumference prior to the onset of gastrulation, b – initiation of DBL, c – DBL develops its own curvature, d – the DBL curvature forces out that of the blastopore circumference; *Bl* – blastopore, for other designations see text. Pointers – cell flows at the blastopore circumference, arrows – cell flows shaping the DBL arc.

of its linear (*Larc*, see Fig. 1, b) and angular (*Aarc*, see Fig. 1, b) lengths. Later on the DBL forms its own curvature which is distinct from that of the blastopore circumference and, starting from this moment, the measurements can be added by the linear height of the DBL arc (*Harc*, see Fig. 1, c), which is a measure of the arc curvature. We consider an interval between the arc formation and its conversion into the semicircular DBL (Figs. 1, b–d). At this interval, one can measure all listed characters and each of them does not change the direction of its temporal change: *Larc*, *Aarc* and *Harc* are subject to increase while the *Lyp* is subject to decrease up to the blastopore closure.

The repetitive homology of changes that occur over the MZ both in space in time becomes evident when we are considering patterns of the mass cell flows (arrows in Fig. 1) molding new shapes of the blastopore circumference. The MZ shape prior to the onset of gastrulation implies that cell flows have normal orientation, that is, the cells move along the tracks that are coincident with the normal radii of curvature of the blastopore circumference (Fig. 1, a). The initial (straight) shape of the DBL means (for the details see Cherdantsev, 2003, 2006; Scobeyeva, 2006) that cell flows deviate from normal orientation to converge in the centre of the DBL line (Fig. 1, b). Their convergence means that they shape the DBL line converting it into the arc with its own curvature. The arc formation normalizes the orientation of cell flows at new radii of curvature, which means deviating from normal orientation of the bordering flows of cells and, consequently, spreading of the DBL in space (Fig. 1, c). New curvature of the blastopore circumference arising with shaping of the DBL arc gradually forces out the initial one (Fig. 1, d). Thus, the DBL arc develops as a spatial unfolding of a single shaping process generating a dorsoventral series of repetitively homological DBL shapes. In a correspondence to the unfolding principle, at one pole of the series is an «older» DBL fragment, whose own developmental history is identical to that of the whole series, and at opposites (lateral) poles are «younger» DBL fragments having no developmental history on their own. Older fragments are «distal» in the sense that their curvature is most remote from the initial one, while younger fragments are «proximal» in the sense that their own curvature is close to the initial curvature of MZ (see Fig. 1).

The relationships between the coefficients of variation of metric characters and their specific rates were studied in fixed embryos of the common frog, *Rana temporaria*, developed synchronously from the eggs of the same clutches spawn in nature. The embryos were reared in the lab at optimal aeration conditions and temperature (18 °C). The first fixation was made just after the DBL had formed its own curvature (see Fig. 2).

The next fixation was made in three hours, when the DBL acquired the crescent-like shape. Each fixation consisted of 300 embryos taken from the same egg clutch. The specific rates of changes were calculated as $V = (M_1 - M_2)/M_1$, where $M_1$ and $M_2$ were the mean values of measurements made in the first and second fixations, and matched to the values of the coefficients of variation (*CV*) calculated for the first fixation.

The arrangement of quantitative characters in the phase space $\{V, CV\}$ shown in Fig. 2 demonstrates a clear-cut positive connection between *CV* and *V* values. The DBL arc height (*Harc*) leading in the amount of both variance and developmental rates is a youngest character, as it arises at later gastrulation stages by bending of the straight DBL

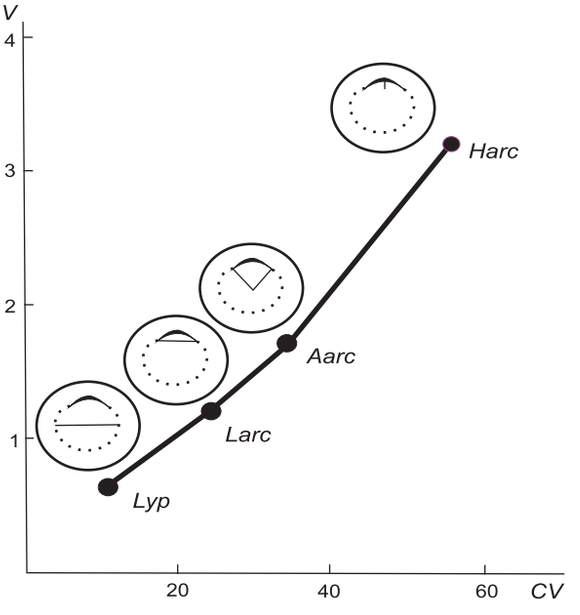


**Fig. 2.** Interdependence between variation and specific rates in the DBL shape characteristics in the frog gastrula.

*CV* (abscissa) – coefficients of variation at the crescent-like DBL arc stage, *V* (ordinate) – specific rates of changes between the crescent-like and semicircular DBL arc stages. Designation of characters is the same as in Fig. 1.

line and, consequently, can develop under the constancy of the characters *Aarc* and *Larc*. The last two characters arise by shaping of a fragment of the blastopore circumference and, as referred to the tangent of this circumference, can develop on their own under the constancy of the MZ diameter (*Lyp*). As for the character *Lyp* having the least variance and slowest developmental rate, it refers to the «oldest» part of the MZ zone whose shape has formed prior to the gastrulation onset.

The additional variance of younger characters, especially *Harc*, is a direct consequence of the convergence of cell flows, which provides an opportunity of changing of the DBL arc curvature under the constancy of its linear and angular lengths. This, in turn, provides a positive feedback between the arc shaping in both space and time. In fact, both the lateral spreading of DBL and the increase in its curvature at the dorsal pole lead to an increase of spatial heterogeneity of the DBL as a whole. This stimulates lateral (youngest) DBL fragments to take over the dorsal ones until the new curvature becomes uniform over the whole DBL. Earlier we have shown (Cherdantsev, 2006; Scobeyeva, 2006) that this occurs just at a transition of DBL from the crescent-like to semicircular shape when the orientation of cell flows normalizes in all DBL fragments (cf. orientation of the cell flows shown in Figs. 1, b–d). It follows that the decrease of variation is not canalization in Waddington's sense. Rather, this is a direct and natural consequence of vanishing of the positive feedback between the local and non-local behavior of the DBL parts.

**Analysis of variance in the individual pathways by repeated measurements of quantitative characters in living embryos.** Up to this point, we have been considering the spatial repeatability of the developing structure. In order to evaluate its temporal component in the explicit form, one needs to have a series of measurements made at the same individuals, which presumes measuring of the living embryos rearing in standardized lab conditions. From the same egg clutches of *R. temporaria* spawned in nature, we selected embryos with the synchronous onset of gastrulation. Selected embryos develop in individual plastic wells at 18 °C. At 40 min intervals, we oriented each individual embryo the vegetal pole upwards and made the photographs at which we measured the metric characters *Lyp*, *Larc*, *Aarc* and *Harc* (see Figs. 1, a–c). In total, we measured 150 embryos from seven egg clutches, each character in each embryos being subject of 5 successive measurements. The mean values of characters we expressed in conventional units equal to 0.05 mm.

The time dynamics of the coefficients of variation (*CV*) and mean values (*M*) of the characters *Harc*, *Larc* and *Aarc* is shown in Fig. 3, the number of a measurement (1–5, abscissa) being the measure of time.

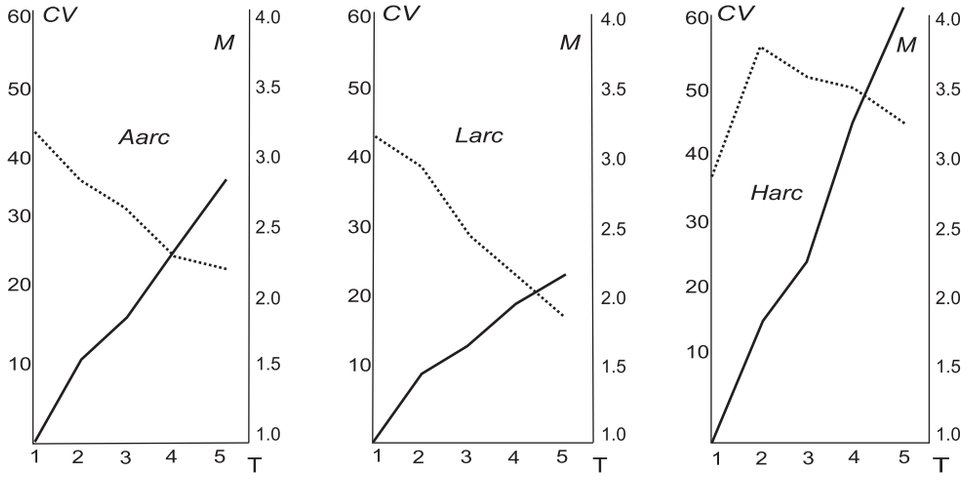


**Fig. 3.** The time dynamics of variation and means in the frog gastrulation.

Abscissa (T): measurements numbers (1–5). Ordinates: coefficients of variation (*CV*, dotted line) and mean values (*M*, solid line) of characters (for designations see text) are shown at corresponding graphics. These data are those of measuring of the living embryos in 40 min intervals from the appearance of the gastral cleft to the semicircular DBL arc. For each character, their mean values are those normalized to the initial means.

The variation is at a highest level at the onset of the DBL arc formation and decreases, as the arc acquires the spatially homogeneous shape, the semicircular one, whose formation roughly corresponds to a measurement number five. Note that for the characters *Aarc* and *Larc* the maximum of variance corresponds to the very beginning of gastrulation when the DBL line has no a curvature on its own. As for the character *Harc*, its variability reaches the maximum just at a stage (see Fig. 1, c) at which the change in the DBL arc curvature becomes the preponderant morphogenetic process. In total, the general variation of the character *Harc* is much higher than that of the characters *Larc* and *Aarc* (cf. Figs. 2, 3).

Thus, as it concerns with the proportion of variability of the characters, the study of successive developmental stages yields the same general results as that of variation in synchronously fixed embryos. The same refers to matching of the variation of characters to their developmental rates. The DBL arc curvature (*Harc*) changes at a much higher rate than the arc linear and angular lengths (*Aarc* and *Larc*).

**A model of morphogenesis based on within-individual selection analog.** Our starting point is that the between-individual differences are reproducible, if (*and only if*) they have a within-individual analog. One can infer an appropriate model from the unfolding principle, as it matches between-individual differences to within-individual ones. We make use of a simple geometric construction shown in Fig. 4, a.

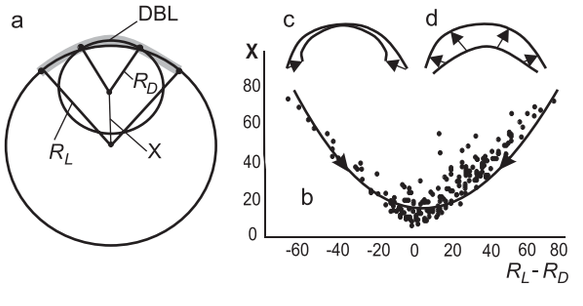


**Fig. 4.** A model of the DBL shaping based on the analysis of variability.

a – partitioning of the DBL arc into younger ($R_L$) and older ($R_D$) circles, b – plot, c and d – DBL shaping modes corresponding to two parabola branches; X – a distance between their centers; pointers – movement vectors of the dynamical system, arrows – cell flows allowing for the corresponding DBL shaping.

In each individual embryo having the crescent-like DBL, we partitioned the arc into three fragments of equal angular lengths, a dorsal (median) one and two lateral fragments that flank the dorsal region. Then, as shown in Fig. 4, a, we constructed two circles, one having a radius close to that of the dorsal region ($R_D$), and the other circle with a radius close to that of the lateral DBL regions ($R_L$). For the simplicity, we assume that both lateral fragments have equal curvature.

The reason for such a construction is the unfolding principle, which permits to consider these circles as corresponding to consecutive stages of the DBL shaping (see Fig. 1). Then, the evolution of shape fits to one-dimensional dynamics of a variable $X$, which is the distance between the centers of «younger» ($R_L$) and «older» ($R_D$) circles shown in Fig. 4, a.

The empirical dependence of $X$ on ($R_L$–$R_D$) obtained from the analyses of variance of the DBL shaping and shown in Fig. 4, b perfectly fits to a parabolic curve in the phase space $\{X, (R_L–R_D)\}$. It follows from the distribution of data that a point at which ($R_L$–$R_D$) and $X$ are also close to zero is an attractor of the dynamical system. This means that the system moves towards minimization of spatial variance of the DBL shape (see pointers in Fig. 4, b}, which, owing to the unfolding principle, is equivalent the achievement of a state at which $dX/dt$ is also equal to zero. The DBL moves to this state by adapting $R_L$ to $R_D$ (Fig. 4, c, a dominating shaping mode), or vice versa (Fig. 4, d, a minor shaping mode) as shown by arrows in corresponding figures.

It follows that, in a rough approximation, $dX/dt = X\,(R_L–R_D)$,

where ($R_L$–$R_D$) is obviously proportional to the amount of within-individual variance in all quantitative characters whose dynamics concerns with the DBL shaping and tends to zero when the DBL acquires a uniform curvature. In general, if, in amphibians, the dorsal pole were not beforehand fixed, we would have had $dX/dt = X\ (R–R^*)$,

where $R$ were a radius of curvature of a given DBL fragment, and $R^*$ – mean radius of curvature of the whole DBL. Again, ($R–R^*$) is obviously proportional to the amount of variance.

Thus, we can conclude that the morphogenetic system moves towards minimization of within-individual variance at a rate proportional to the

amount of variance, which is mathematically indistinguishable from what Fisher's «Fundamental Theorem of Natural Selection» states.

## Conclusion

The above data show that within-individual variability inherent to normal dynamics of morphogenesis is the main source of between-individual differences that are highly reproducible with no respect to a contribution of both the additive genetic variance and fitness. As a dynamical system, morphogenesis is subject to the same mathematical principles as those of selection, where the notion of fitness is absent being replaced by the account of relationships between the shapes of embryonic areas involved into the same shaping process. Among a variety of shaping trends, each embryonic area selects those that can be readily continued by neighboring areas. The situation is very similar to that arising in fallacious genetic experiments in which the animals with better characteristics get the better diet. In our case, this is a premise to within-individual selection based exclusively on differential capacity of different shapes of the areas to involve surroundings into their own shaping. An opportunity of this kind of selection means, first, that selection is a wider concept than fitness and, second, that the shape of a developing area carries information on its developmental trend.

It follows, in particular, that it is erroneous to identify the dynamics of inherent developmental variation (IDV) with developmental canalization. The reason why variation decreases with approximating of the form to the eventual state lies not in the enhancement of regulation, but rather in the exhausting of within-individual variation component allowing for both the direction and rate of morphological changes.

What is worthy to stress is that the within-individual component of variation, owing to the unfolding principle, is reproducible despite its inheritance and contribution to fitness may be close to zero. Then, insofar as within-individual differences manifest at individual level, they might correspond to what Darwin understated under the vague term of «indefinite» variation (cf. Cherdantsev *et al*., 1996).

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