Journal of Evolutionary Science

Ontogenes in Drosophila Melanogaster and a Model of Speciation

B.F. Chadov[1,*], N.B. Fedorova[1]

[1]Institute of Cytology and Genetics, Siberian Branch, Russian Academy of Sciences, Novosibirsk, 630090 Russian Federation

Abstract

A new type of mutations-dominant lethals with a facultative manifestation -were discovered in *D. melanogaster* in 2000. These mutations were named conditional mutations. Under restrictive genetic conditions, the mutations manifest themselves as dominant lethals, whereas dominant lethality disappears under permissive conditions, displaying a set of other manifestations. The genes responsible for the emergence of conditional mutations were named ontogenes. The experiments with mutations in ontogenes have revealed the following processes: (1) genome editing in germline cells; (2) induction of high mutagenesis rates in germline cells of the mutants for ontogenes; (3) zygotic selection; (4) isolation of mutants; and (5) alterations in the lethality of mutants with time. The specific features in the manifestation of ontogenes together with the listed processes formed the background for construction of the model of speciation named the regeneration model. The event of speciation is represented as the regeneration of the working state of a genetic system disturbed by the emergence of a mutation in an ontogene. According to the model, it is ontogenes that are in charge of speciation and, eventually, the structure of living matter in the form of individual species. The significance of Mendelian protein-coding genes and Darwinian selection of the fittest according to these genes are doubtless but not paramount.

Research Article

Open Access &

Peer-Reviewed Article

DOI: 10.14302/issn.2689-4602.jes-24-4956

Corresponding author:

B.F. Chadov, Institute of Cytology and Genetics, Siberian Branch, Russian Academy of Sciences, Novosibirsk, 630090 Russian Federation

Keywords:

Darwinian selection, zygotic selection, isolation, regeneration model of speciation, drosophila

Received: February 2, 2024

Accepted: March 9, 2024

Published: March 13, 2024

Citation:

B.F. Chadov, N.B. Fedorova (2024) Ontogenes in Drosophila Melanogaster and a Model of Speciation. Journal of Evolutionary Science - 1(3):35-58. https://doi.org/10.14302/issn.2689-4602.jes-24-4956

Introduction

A living organism not only exists and reproduces, but also is actively involved in *the evolution of the living* in cooperation with the individuals of its species. The goal of biology is to determine the elementary structures and events of evolution, the process unique in its duration and results. One of the events (factors) of evolution is selection of the fittest, discovered by Charles Darwin. The fitter an individual to its habitat, the more numerous is its offspring and the higher, according to Darwin, its contribution to the next generation. The selection of the fittest among breeder organisms is constantly going on (being a *natural* process) and is able, according to Darwin, to lead to the emergence of a new species [1].

The modern synthesis of evolutionary theory unites the Darwinian idea of natural selection with genetics. It regards *gene mutation* as another elementary event in the evolutionary process. According to the synthesis of evolutionary theory, the emergence of a new species is the selection of genetic mutations that increase the

fitness of an organism. In this theory, the complete set of elementary factors of evolution comprises (1) mutation process, (2) population waves, (3) isolation, and (4) natural selection [2].

Indeed, the selection of the fittest explains the harmony between an organism and environment that develops in the course of evolution but the content of evolution extends beyond this. Evolution implies an increase in the complexity of organism [3]. An increase in the complexity of living organisms on a historical time scale is a commonly recognized fact, first uttered by Herbert Spenser [4]. The ladder of living beings (*scala naturae*) is the symbol of biological evolution. The presence of a particular taxon in the ladder indicates the presence of certain kind of fitness. If so, fitness cannot reflect the degree of evolutionary advance for mere logical reasons.

The transfer from the selection of characters to the selection of mutations is one step further towards the understanding of speciation but not yet the resolution of the problem. Mendelian mutations, regarded as the factors of evolution, are unable to implement the processes that the synthetic theory of evolution itself regards as necessary for the course of evolution [2]. Although Mendelian mutations are the objects of natural selection, they (1) are too infrequent to form the complexes necessary for the formation of biological characters, (2) are not inducers of mutagenesis, and (3) cannot create isolation [5].

It was quite unexpected that the protein-coding (Mendelian) genes, used in evolutionary constructs, are not the only and universal hereditary units. New mutations were generated in *D. melanogaster* [6, 7] and later named conditional mutations [8, 9]. Under the restrictive genetic conditions, mutations appear as dominant lethals and under permissive conditions, the dominant lethality disappears, while other manifestations emerge, namely, (1) recessive lethality; (2) altered visible phenotype; (3) meiotic nondisjunction of chromosomes; (4) development of monstrosities (morphoses); (5) increase in the basal metabolism and locomotor activity; and so on [8, 9]. The genes responsible for the formation of conditional mutations were named ontogenes in the view of the formed morphoses [10]. As might be expected, the genes of this new category are the particular genetic material that is lacking for the arrangement of evolutionary process.

As far as the research into conditional mutations was going on, the involvement of ontogenes in evolution was becoming ever more clear [11–14]. The ontogenes allowed the role of chromosomal rearrangements in speciation [15, 16] to be explained, as well as the significance of genomic instability for evolution [17, 18]. Three following cardinal problems in speciation are theoretically resolvable with the help of ontogenes: (1) speciation as a multistep mutation process; (2) the role of selection in speciation; and (3) the mechanism underlying the establishment of isolation [5]. These three problems were long defined, have been studied and described in numerous papers, but remained unsolved until recently [19–23].

The existence of zygotic selection is of special importance for the insight into evolution [24, 25]. This is a novel type of selection, which coexists with the Darwinian selection but differs from it in the underlying mechanism. After a successful fertilization, the zygote **"decides"** on whether it continues to develop or not depending on the interactions between the parental pronuclei. Unlike the Darwinian selection, the habitat of an organism does not determine this type of selection. This type of selection rather appears as a constantly ongoing autogenesis (orthogenesis or nomogenesis) of the living beings. Here, the question arises on what is the criterion for zygotic selection if it is not environment.

Concurrently with the consideration of evolutionary challenges in terms of ontogenes, we have discovered new data on the ontogenes themselves. The most important of them are (1) the similarity

between the manifestation of mutations in ontogenes and the phenomenology of genetic incompatibility in distant hybridization [26]; (2) the role of ontogenes in the construction of cell ensembles [27, 28]; and (3) the existence of remote interaction between ontogenes [28–31]. These data clarify the role of ontogenes in evolution. The goal of this paper is to present the concept of speciation relying on the information obtained while studying ontogenes. The described model can be referred to as *"the process of regeneration of species-specific program of individual development after it has been damaged by a mutation in an ontogene"*. This is the first presentation of the model. To simplify the understanding of the main idea, we omitted some details in argumentation, which are available in the corresponding references.

Manifestation of mutations in the ontogenes in D. melanogaster

The history of generation of mutations in ontogenes commenced from the idea to partition the biological traits by distinguishing between the traits of intraspecific similarity and those of intraspecific differences. The former are inherent in each individual of a species, determine the outlook of the species, and distinguish it from the other species. The latter are present in some representatives of a species but are absent in the others. The Mendelian protein-coding genes fit the role of the latter [11, 12, 32].

We constructed the "genetic portrait" of the genes responsible for the buildup of the characters that determine the intraspecific similarity. The mutations in these genes seem rather paradoxical: they have to be *viable in homozygote and lethal in heterozygote* (dominant lethals) [11, 12, 32]. New hybridization techniques allowed us to isolate the target mutations in different chromosomes and in large amounts from the irradiated *D. melanogaster* individuals [6, 7, 33]. The collection of mutations became the source of vast and unusual information about the new category of genes [8, 9]. Some mutation manifestations gave us the idea about the feasibility of building up a logical construction referred to as *the model of speciation.* Find below the description of these manifestations and the logic used for the construction of this model named the *regeneration model of speciation.*

Facultative dominant lethality

Table 1 lists the progenies of the drosophila males carrying the generated mutations in their X chromosome. The viable mutant males in the crosses with *yellow* females do not produce daughters, that is, the mutation in daughters acts as a dominant lethal although it manifests no lethality in the male genome of the fathers. Table 2 shows the results of crosses of the same mutant males with the females differing form the females used in the first set of crosses by the presence of the *In*(1) *Muller-5, w^a B* inversion in one of the X chromosomes. This inversion emerged to be sufficient for the mutation to lose its dominant lethality in daughters. Both classes of daughters (+ and *B*/+) appeared in the progeny. Thus, these mutations in the X chromosome manifest themselves as dominant lethals only when the mutant paternal X chromosomes meet with the X chromosomes of *yellow* females. The presence of the X inversion in a female is sufficient for the mutation to lose its dominant lethal effect.

The elimination of a lethal effect of the mutations in the test cross with *yellow* strain repeats if the mutant males are crossed with females (1) *In* (1)5*, y/y,* (2*) In (1)23, y/y***,** (3*) T (1; 2)12 y/y,* and (4) *T* (1; 2)19, *y/y,* carrying chromosomal rearrangements in the *yellow* strain or females of other (wild type) strains *Berlin wild* and *Barnaul* [11]. The lethal effect of these mutations is also eliminated in the case when female crossed with a mutant male carries the chromosomal rearrangements not in the

Table 1. Progenies and fecundity of mutant (+) males crossed with yellow females [26]

Mutant male stock no.	Cross 2♀*y* × ♂+		Cross 6♀*y* × ♂+		Fecundity of male*
	Total number of progenies	Share of daughters in progeny	Total number of progenies	Share of daughters in progeny	
1	119	0.00	191	0.00	0.02
2	650	0.00	435	0.00	0.15
3	112	0.00	180	0.00	0.12
4	114	0.00	293	0.00	0.07
5	50	0.00	303	0.02	0.14
6	47	0.00	283	0.02	0.14
7	47	0.02	100	0.00	–
9	182	0.07	529	0.00	0.40
10	162	0.03	297	0.04	0.09
27	68	0.00	93	0.00	0.18
29	15	0.07	61	0.00	0.14
30	122	0.00	115	0.00	0.19
31	106	0.00	83	0.00	0.15
32	81	0.00	117	0.00	0.13
33	144	0.00	90	0.00	0.16
34	88	0.00	110	0.00	0.12
26	92	0.03	89	0.01	–
35	102	0.03	115	0.04	0.35
36	95	0.00	110	0.01	0.14
37	52	0.02	68	0.04	0.14
38	54	0.06	84	0.01	0.10

* Ratio of adult progenies to the number of laid eggs.

Table 2. Progeny of the crosses of females In(1) Muller-5, wa B/y with mutant males (+) [8]

Male stock no.	Phenotype of progeny				Total
	Daughters		Sons		
	+	*B*/+	w^a *B*	*y*	
1	1	7	127	46	181
2	11	21	47	89	168
4	5	12	77	167	261
5	22	31	36	71	160
6	9	26	58	62	155
30	31	41	86	109	267
31	16	33	65	79	193
32	42	51	60	81	234
33	23	23	61	88	195
34	6	11	44	72	133
36	21	25	58	108	212
Total	187	281	719	972	2159

X chromosome but in the chromosomes of the second and third pairs (females *y*/*y*; +/*Cy,* females y/y; +/*Pm* and females *y*/*y;* +/*D*) [8].

Not only mutations in the X chromosome, but also mutations in other chromosomes manifest themselves as a "facultative dominant lethal". The ability of a mutation to cause lethality under certain genotypic conditions and to fail to manifest it under other conditions has allowed us to design different techniques for generating facultative dominant lethals, including the mutations in chromosomes 2 and 3. Table 3 shows the progeny of facultative dominant lethals in drosophila chromosome 2. Characteristic of the lethals of this type is that they manifest dominant lethality in the compound with a structurally normal autosome 2 but do not manifest it if the opposite chromosome carries the 2 *In*(2*LR*) *SM*1 inversion [33].

The facultative dominant lethals represent the class of mutations the genetics encountered for the first time. By definition, any individual carrying a dominant lethal cannot exist at all. The facts that the mutations with the features of a dominant lethal are obtained and do exist as stocks is explainable by a

Table 3. Progenies of the males and females carrying a dominant lethal in chromosome 2 (reciprocal crossing) [33]

Mutation in autosome 2 no.	♀ *y* × ♂ 2*/*Cy Bl L*^{4}		♀2*/*Cy Bl L*^{4} × ♂ *y*	
	Total number of progenies	Share of individuals (+) with mutation	Total number of progenies	Share of individuals (+) with mutation
7a	226	0.00	162	0.46
37a	254	0.00	158	0.51
44a	234	0.00	161	0.40
53a	231	0.00	239	0.47
5a	303	0.06	206	0.50
8a	239	0.03	94	0.38
9a	198	0.09	89	0.43
62a	300	0.01	104	0.44
Control				
42a	505	0.51	–	–
26a	447	0.53	–	–

* Chromosome carrying mutation.

Table 4. Difference in the manifestation of a Mendelian gene and an ontogene

Type of gene	Normal gene sequence	Mutant gene sequence	
Mendelian gene	Normal phenotype	Mutant phenotype	
ontogene	Normal phenotype	Phenomenology of mutation in restrictive genotype (lethality, no individual)	Phenomenology of mutation in permissive genotype (mutant individual)

facultative character of their dominant lethality. In certain genetic surroundings (ensemble), a mutant ontogene manifests itself as a dominant lethal and the corresponding individual dies in heterozygote; however, it survives, exists in full, and gives progeny in other surroundings. Some genetic conditions that abolish a lethal behavior of the ontogene, such as chromosomal rearrangement and sex of mutant, are shown above. The overall experimental work with the mutations in ontogenes has been performed with the stocks in which the dominant lethality is removed using a particular technique.

The specific functional features of ontogenes able to form facultative dominant lethals are briefed in Table 4 versus the function of a Mendelian protein-coding gene. They are structurally similar since both are represented by DNA regions but are functionally distinct. Being changed (mutated), Mendelian gene creates a single mutant variant, whereas ontogene creates two variants. One of the latter is a lethal (a step towards isolation) and the other variant represents a retained mutation capable of further alterations. Thus, it is clear that ontogene, even in formal terms, has more opportunities to influence evolution. These opportunities are considered in detail below.

Parental inheritance of mutation manifestation

Characteristic of the facultative dominant mutations is a parental pattern of inheritance. In the crosses of the males carrying a mutation in the X chromosome with *yellow* females (Table 1), not only the absence of daughters in the progeny attracts attention, but also a high level of undeveloped eggs. In the case all daughters die, this level must not exceed 50%; however, it was considerably higher for the majority of mutations. This reasonably suggests that not only daughters, but also sons were among the lethals. The latter have not received the mutation from their father but nonetheless died. The transfer of a trait from father to its progeny without the transfer of the corresponding mutation is a manifestation of the parental effect.

The interaction between mutations and chromosomal rearrangements (Table 5) follows a typical parental pattern of inheritance. The progeny of mutant males crossed with *yellow* females lacks daughters, which appear if the mother females carry inversions in autosomes: *In*(2*LR*)*Cy*, *In*(2*LR*)*Pm.* or *In*(3*LR*)*D.* Thus, the inversion in mother's genome partially eliminates the lethal effect of mutation. Interestingly, the presence of inversion in the survived zygote is not obligatory for the removal of lethality. Survived zygotes have either phenotype *Cy* (containing the inversion of mother) or phenotype *Cy*+ (lacking the inversion of mother), as well as *Pm* and *Pm*+. Obviously, here is a typical parental (in this case, female) effect of chromosomal inversion in chromosome 2 on the manifestation of mutation received by daughter from its father.

Of interest is another form of the parental effect observable in the case of interaction between the rearrangements in autosomes and mutations in the X chromosome [32] (Table 6).-In this experiment, males carried both rearrangements and mutations. In this combination, the rearrangements failed to cause the effect. The males crossed with *yellow* females gave no daughters in their progeny although the mutations in the zygote were present together with the studied chromosomal rearrangement *In*(2*LR*) *Cy* (Table 6). Thus, the removal of lethal mutation manifestation by the rearrangement depends on the particular parent from which it was received as well.

As of today, the complete list of manifestations of the mutations in ontogenes comprises seven variants: (1) facultative dominant lethality; (2) facultative recessive lethality; (3) dominant effect on metabolism and activity; (4) dominant effect on meiosis; (5) dominant generation of morphoses; (6) dominant generation of instability; and (7) dominant type of modification of ontogene manifestations (rearrangements in heterozygote). The parental pattern of inheritance in different variants is

Table 5. Effect of rearranged chromosomes 2 and 3 on the conditional dominant lethals in the X chromosome delivered to the zygote with sperm (crosses of mutant males with females (1) y/y; +/+; (2) y/y; +/In(2LR)Cy; (3) y/y;+/In(2LR)Pm 4; and (4) y/y; +/In(3LR)D [8]

Male Mutant stock	Female y/y; +/+		Female y/y; +/Cy				Female y/y; +/Pm				Female y/y; +/D			
	Daughter +	Son y	Daughter +		Son		Daughter		Son		Daughter		Son	
			Cy+	Cy	Cy+	*Cy*	*Pm*+	Pm	*Pm*	Pm	*D*+	*D*	*D*+	*D*
1	–	230	–	–	178	163	–	–	107	57	–	–	115	8
2	–	230	14	13	127	134	4	3	70	72	–	–	42	7
4	–	270	9	4	185	159	1	7	86	81	–	–	162	7
5	–	197	23	21	80	95	6	4	47	48	–	–	37	3
27	2	167	1	0	102	113	2	1	53	65	–	–	9	2
29	4	163	32	27	71	56	26	24	55	20	6	6	88	10
30	–	184	15	13	81	76	9	12	60	47	–	–	38	6
31	–	242	32	20	127	102	5	4	28	29	–	–	70	6
32	–	197	22	10	90	77	9	17	36	32	–	–	48	2
33	–	209	20	18	95	101	11	8	87	47	24	2	85	12
34	–	140	11	14	88	101	25	20	68	54	–	10	103	3

Table 6. Effect of complex inversion In (2LR) Cy, Cy in male autosomes 2 on the penetrance of lethal in the X chromosome [32]

Male stock no.	Phenotypes of progenies			
	Cross ♀ *y* × ♂+		Cross ♀ *y* × ♂ +; *In*(2*LR*) *Cy*/+	
	♀ +	♂ **y**	♀ +	♂ **y**
2	–	59	–	14
4	–	125	1	137
5	–	95	–	144
26	–	56	–	43
30	–	77	–	49
31	–	114	–	137
32	–	55	–	82
33	–	66	–	54
34	–	41	–	14
36	–	89	–	140

characteristic of all seven manifestations [31, 34–37] although only three cases, associated with manifestations (1) and (7), are described above for the sake of brevity.

A parental pattern of inheritance is a consequence of the gene activity in a germinal cell. The initial mutation and the "product of its activity" during the reduction division in meiosis are distributed independently of one another to give the gametes carrying the "product of activity" but lacking the mutation that is its source. In terms of phenomenology, the formation of the gametes of this type gives

the progenies that received the parental character without receiving the correspondingly gene (parental pattern of inheritance) [35]. The parental pattern of inheritance of mutant manifestations in an ontogene suggests that (1) *ontogenes are active in germline cells,* (2) *they interact with other ontogenes,* and (3) *the interaction leaves a "trails", which are delivered together with the gamete.* Numerous cases of paternal parental effect (in particular, shown in Table 1) that exclude the transfer of the cytoplasm components of the sperm to the zygote suggest that the parental effect of an ontogene is determined by the changes in the conformation of other ontogenes.

Induction of genetic instability

The observations of mutations in ontogenes in permissive stocks have supplied us with extensive information about the specific features in mutation manifestations. One of the key specific features of mutants is their physiological and genetic instability. Find below six arguments favoring this inference.

Development of morphoses, modifications, mosaics, and gynandromorphs. Many mutations have been found to give rise to phenotypically abnormal progeny. Generally, these abnormalities are morphoses affecting various body parts; they are mainly asymmetric and uninheritable. Both the maternal and paternal effects are observable in the development of morphoses. In four cases, dimorphic mutations are recorded, namely, a female homozygous for a mutation had a mutant phenotype, while its male counterpart was phenotypically normal. The mutations are recessive with regard to the norm. New phenotypes behaving as mutations with incomplete penetrance emerged during cultivation. In the stocks of mutant homozygotes, numerous phenocopies emerge, persist for one or two generations, and disappear. One wave of phenocopies followed the other. The emerging visible phenotypes further behave as ordinary recessive mutations [38–40].

Loss in manifestation of a dominant mutation in the opposite chromosome. Characteristic of the lethal mutations in autosome 2, maintained in heterozygote with inverted chromosome *In*(2*LR*)*Cy*, *Cy Bl* L^4, is the "loss" in manifestation of dominant mutations *Cy* , *Bl,* and L^4 in the inverted chromosome (Fig. 1). The loss takes place in the crosses aimed at maintenance of mutations and in the crosses between mutant stocks [8]. Over the first half year of mutation maintenance, 20 cases of the loss in manifestation were recorded (Fig. 1): one marker was lost in 17 cases and two markers (*Cy, Bl,* and L^4 individuals) in three cases. The reciprocal classes sharply differ in the abundance, suggesting that the nature of the losses is not related to crossing over. The chromosomes with the altered set of dominant markers continue acting as the balancers of lethals in autosome 2. This is another argument against a crossing-over nature of the losses. The loss in dominance manifestation for each of the three mutations was autonomous. That is why the loss in one mutation was the most frequent and in two, less often. Any case of the loss in all three mutations was unobservable. Each of the mutations was lost separately but at different rates. The *Curly* mutation was lost in 11 cases; *Lobe,* in 10; and *Bristle,* in two cases.

The rate of loss in manifestation was high. Six cases of nonmanifestation among 90 progenies (rate, 6.7%) were recorded in the crosses of two lethal stocks (nos. 37 and 53). However, any case of the loss in marker was unobservable among 833 progenies in the cross of *yellow* females with mutant males (four stocks). Over several decades when the *In*(2*LR*)*Cy*, *Cy Bl* L^4 chromosome was retained in laboratory stocks, any cases of the loss in manifestation of dominant markers have not been recorded. Correspondingly, we believe that mutations in ontogenes were the actual reason underlying the loss in dominant mutations in the *In*(2*LR*)*Cy*, *Cy Bl* L^4 inverted chromosome.

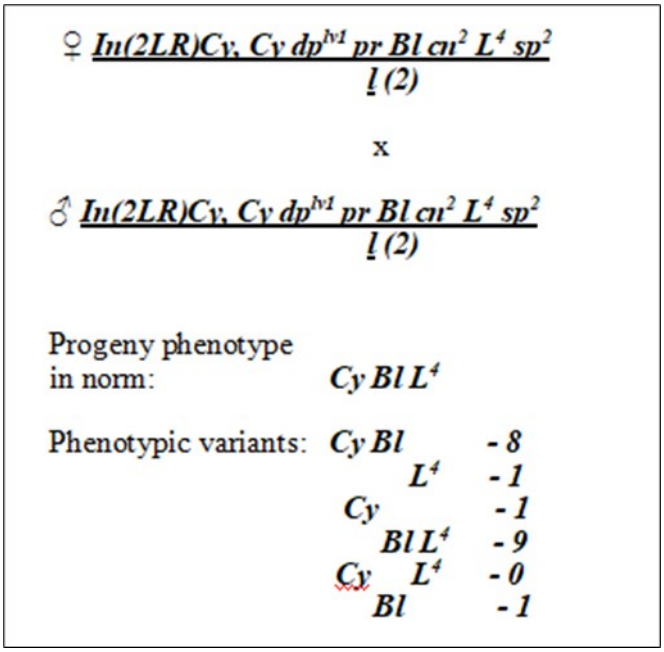

Figure 1. Nonmanifestation of the phenotype of dominant mutations in autosome 2 [8].

Lethal mutations *l*(2) in autosome 2 were maintained in the stock with the inverted autosome 2 carrying dominant mutations *Curly* (*Cy*), *Bristle* (*Bl*), and *Lobe* (L^4). In the norm, the progenies manifested all three dominant mutations; however, the loss in manifestation of one or two mutations was observed in 20 cases.

Secondary mutagenesis. The lethals were mapped using a standard set of deletions for 10 mutations in ontogenes displaying a recessive lethality in chromosome 2. Five mutations had two and more lethal defects. The multiple lethal defects of an individual mutation are unexplainable with the statistics of γ-irradiation. One of the mutations with four lethal regions had a *small barrel* (*Smba*) visible phenotype. The *Smba* phenotype in the *Smba*/*In*(2*LR*)*Cy* strain is inherited according to the parental pattern but disappears in the *Smba*/*In*(2*LR*)*Pm* strain. In the same strain, lethality is lost in one of the four initially lethal regions. In a separate experiment, we observed how the mentioned region commenced to lose the lethal manifestation after introducing the *In*(2*LR*)*Pm* chromosome into the *Smba*/*In*(2*LR*)*Cy* strain. We also observed the process of loss in *Smba* phenotype in three substocks of the *Smba*/*In*(2*LR*)*Cy* stock after its cross with the *Smba*/*In*(2*LR*)*Pm* strain over 13 successive generations. In our view, the regions of multiple recessive lethality repeatedly (secondarily) emerge under the influence of a radiation-induced mutation in ontogene [41].

Transposition of mobile element 412. This study involved two strains carrying mutations in ontogenes in the X chromosome. The strains were dimorphic: only females displayed the mutant phenotype, whereas the males were normal. Multiple transpositions of retrotransposon 412 were observed in the strains. The rates of inversions exceeded those for isogenization, a strong inducer of MGE (mobile genetic element) transposition [42].

Disturbances of meiosis and mitosis. In total, 30 mutations in ontogenes located in the *D. melanogaster* X chromosome were assayed for their ability to cause the meiotic nondisjunction of X chromosomes [31]. The level of X nondisjunction in the females heterozygous for mutation in ontogene emerged to

be very high. The share of matroclinous daughters reached 24.7% of the total progeny and of patroclinous males, 24.9%. An inversion in the opposite X chromosome and additional Y chromosome had no effect on the X nondisjunction. The balance between XX and X0 egg cells was disturbed: exclusively daughters were prevalent in the females with a normal opposite X chromosome versus the females with inverted X chromosome, displaying the prevalence of sons. Moreover, 12% of the matroclinous daughters produced by the mothers with a normal opposite X chromosome appeared to be homozygous for the marker of one of the maternal X chromosomes (equational nondisjunction). A "damping" parental effect of a mutation in ontogene on the X chromosome nondisjunction was observed [31].

Increase in basal metabolism and locomotor activity of mutants. An unusually high mobility and a high sexual activity of mutant males were recorded. The energy metabolism of mutants was assessed using special tests. For this purpose, it was measured in the flies of four mutant and four control strains with indirect calorimetry (according to the emitted CO_2). In addition, a special device was used to assess the locomotor activity of these flies. The energy metabolism and locomotor activity of the mutants were higher as compared with the control in a statistically significant manner [8, 9, 43].

The above data demonstrate a physiological and genetic instability caused by the presence of a mutation in ontogene. Section 1.5 will consider the data on the changes in the lethality of mutations over their cultivation in laboratory. They supplement the body of the data on the instability in mutant stocks.

Phenomenon of death at the stage of zygote

In the genetic experiments with drosophila, the death of a few laid eggs does not attract any attention. This can be caused by failed fertilization or a chromosomal rearrangement received by a progeny, which disrupted its viability. The following facts were observed in the crosses of mutants for ontogenes: (1) a very high level of egg death (Table 1) (2) for the overwhelming majority of mutations (3) in heterozygous state. Undoubtedly, we encountered an outstanding phenomenon determined by the specificity of mutations. In the experiment with *yellow* females, we determined the critical phase in lethality for 18 mutations in the X chromosome (Table 7). This experiment allowed us to assess the death rate at the stages of (1) white egg, (2) brown egg, (3) larva, (4) pupa, and (5) imago. The egg samples were obtained from assuredly fertilized females. The death took place at the stage of egg in 90% of the cases (72%, at the stage of white egg and 18%, brown egg). The stage of white egg matches the zygote containing two pronuclei to syngamy and of brown egg, the first stages of embryonic development after syngamy. Thus, the disturbance of the events taking place immediately before the syngamy kills the mutants [36, 37, 44]. The details of this phenomenon are described when discussing it in Section 2 "Critical events of speciation performed by mutant ontogenes".

Processing of lethal mutation manifestation in generations of permissive stocks. The instability of permissive stocks, mentioned in Section 1.4, had one more specific feature, namely, it changed with time. In particular, the rate of the individuals with monstrosities decreased with the duration of stock cultivation. A change in the cross mate again increase the yield of monstrosities; however, the trend of a decrease yet retains. The other mutation manifestations underwent changes as well. We succeeded in recording the changes with time for some of them.

Loss in dominant lethal with time (delethalization). The loss in a dominant lethal effect of mutations was accidentally discovered in 2001 in the experiments on determining the rate of dominant lethals. The males from stocks nos. 1, 3, 5, 27, and 33, maintained using the attached X chromosomes,

Table 7. Lethality of zygotes in the crosses of yellow females with the males carrying conditional mutations in the X chromosome [36]

Male mutant stock no.	Total number of laid eggs	Lethality (%) at the stage of				Viable imagoes (%)
		White egg	Brown egg	Larva	Pupa	
1	50	92	2	–	–	6
2	50	81	13	2	–	4
3	50	76	18	–	–	6
5	100	65	28	3	–	4
6	50	80	8	–	–	12
7	50	52	32	6	2	8
8	50	90	6	–	–	4
10	50	68	20	6	–	6
11	50	56	30	2	–	12
27	50	72	8	6	–	12
29	50	92	6	–	–	2
30	50	96	2	1	–	–
31	50	90	4	2	-	4
32	50	46	32	8	–	14
33	50	50	28	6	2	14
36	24	33	54	–	6	7
38	40	68	22	5	–	5
41	50	90	6	–	–	4
Mean	51	72	18	3	0.6	7

commenced to give daughters in the crosses with *yellow* females (Table 1). In the following years, the lethality was tested using more representative samples of progenies. Five of the above-mentioned mutations, tested in 2002 and 2004, demonstrated that they actually lost their lethality. In 2002, three additional mutations (nos. 29, 38, and 41) lost their lethal effect and one more (no. 35), in 2004. Lethality did not disappear but decreased in some stocks so that daughters appeared in the progeny although their share did not reach the expected level of 50% (nos. 7 and 9–11). In total, nine of the 23 mutations completely lost their lethality and four turned semilethal [17, 18].

The delethalization of mutations nos. 1–41 took place in the stocks maintained in heterozygote with the Muller-5 chromosome. Over the same time interval, eight mutations (nos. 3, 5, 9–11, 32, 34, and 38) completely lost their lethality and eight mutations (nos. 6–8, 30, 31, 33, 35, and 36) decreased it. The difference in the techniques used for maintaining mutations definitely influenced delethalization. The

Muller-5 stock preserved mutations more reliably. After the loss in lethality and its sharp decrease in some stocks were discovered in 2002, ten stocks maintained using attached X chromosomes were duplicated by new stocks obtained from the males of the corresponding Muller-5 stocks, which retained the lethality of mutations. By 2004, seven mutations of the ten, that time maintained using attached X chromosomes, once again lost their lethality. Only three of them retained the lethality in both cases, including the maintenance using the Muller-5 chromosomes. These data suggest that the properties of mutations did change in stocks. This process depends on both the mutation itself and its genome surroundings [17, 18].

Loss in recessive lethality (homozygotization of mutation). In the previous section, we referred to the loss in a dominant lethal manifestation by a mutation in the cross of mutant male and *yellow* female as *delethalization*. This cross repeats the test cross for detection of mutations. The occurred delethalization refers only to dominant lethality, while recessive lethal manifestation of mutation remains. However, the cases of the loss in this type of lethality appeared in the further maintenance of the X-chromosome mutations in the +/*In*(1) Muller-5, *B, w*^{a}. They were easily recognizable according to the emergence of +/+ females. The first +/+ females were completely sterile,; with time, weakly fertile females started to appear as well. Thus, we can assert that a lethal manifestation of mutations is lost with time (thereby restoring fertility). This process develops in a stepwise manner: (1) first, only facultative dominant lethality disappears (2) followed by weakening of recessive lethality with emergence of homozygotes for mutation, and, finally, (3) sterility disappears in the homozygotes for mutation so that they become fertile. Unfortunately, the phenomenon of the loss in lethality is rather infrequent and we have no adequate statistics for this phenomenon. This process is of a fundamental importance and will be discussed in the next sections.

Critical events of speciation performed by mutant ontogenes

The synthesis of evolutionary theory in one of its variants specified the following factors of evolution: (1) mutation process; (2) isolation; (3) natural selection; and (4) population waves [2]. The mutation in gene is regarded as the *elementary structure* of evolution. The pattern of manifestation of ontogenes described in the previous section comprises many episodes that the synthesis of evolutionary theory ascribed to speciation, in particular, the induction of mutagenesis caused by a primary mutation, zygotic selection in the form of the eggs with arrested development, and emergence of morphological novelties in the form of morphoses. As is mentioned above, once the mutations in Mendelian genes are unable to implement the processes that the synthetic theory states necessary for speciation [5], the ontogenes, as is suggested by the manifestation of their mutations, can well turn out the appropriate but missing tool for implementation of the tasks related to speciation. Three of the processes suggested by the synthetic theory to lead to speciation are key factors: selection, mutagenesis, and isolation. See below that all these three processes can be performed by ontogenes.

Zygotic selection

Darwinian natural selection goes on under the action of environment among the adult sexually mature breeder organisms. The selection among the mutants for ontogenes also takes place but at the stage of zygote. At this stage of individual development, it is out of question to speak about the effect of environment because the multicellular organism as such does not yet exist. Zygotic selection is a pure autogenesis (nomogenesis or orthogenesis as synonyms) organized and controlled by the genetic system itself. The evolution of the living beings in this case is inspired by the living itself and its tool is

Table 8. Loss in lethal manifetation of the mutations generated in 2000 (maintained in an attached X stocks) [17]

Stock no.	2000		2001		2002		2004	
	Total progenies	Share of daugh-ters	Total proge-nies	Share of daugh-ters	Total proge-nies	Share of daugh-ters	Total progenies	Share of daughters
1	191	0.00	13	*0.46	199	*0.42	77	*0.52
2	435	0.00	4	0.00	259	0.02	36	0.03
3	180	0.00	20	*0.45	311	*0.43	95	*0.50
5	303	0.02	33	*0.45	265	*0.60	83	*0.41
6	283	0.02	2	0.00	111	*0.02	39	0.05
7	100	0.00	3	0.00	44	**0.27	63	**0.40
8	216	0.07	5	0.00	90	0.09	49	**0.14
9	529	0.00	7	0.00	169	**0.21	81	0.04
10	297	0.04	7	0.00	69	**0.30	57	**0.26
11	409	0.06	4	0.00	82	**0.18	55	**0.16
26	89	0.01	–	0.00	175	0.07	40	0.02
27	161	0.00	29	*0.69	113	*0.56	92	*0.49
29	76	0.00	4	0.00	171	*0.54	80	*0.51
30	115	0.00	8	0.00	109	0.02	71	0.00
31	189	0.00	8	0.00	138	0.01	70	0.03
32	198	0.00	4	0.00	74	0.00	53	0.02
33	234	0.00	23	*0.52	214	*0.56	88	*0.51
34	198	0.00	–	0.00	62	0.00	54	0.02
35	115	0.04	12	0.00	162	**0.13	83	*0.48
36	110	0.01	5	0.00	106	0.02	54	0.07
38	84	0.01	3	0.00	80	*0.56	51	**0.33
41	100	0.01	5	0.00	331	*0.49	106	*0.52

* Loss of a lethal effect of mutation and ** decrease in a lethal effect of mutation.

the genetic system of the living.

The methodology of the zygotic selection is more intricate. The selection according to Darwin is the summation of mutations in the generations and each of mutations contributes to an increase in fitness. The summation does not alter the quality of the selected material but changes its quantity. Zygotic selection operates with facultative dominant lethals. In this process, not the primary mutations are the object of selection but rather genetic supplements to them that protects the mutation against elimination. In the former case, the supplement discards dominant lethality and in the other, does not discard it. In the former case, zygotic selection allows a mutation in ontogene together with the supplement to continue its life, eventually giving rise to the adult progeny carrying the mutation in ontogene in a permissive genotype. In the latter case, the life process is arrested, resulting in a fertilized white egg that ceased to develop.

The final biological effects caused by selection are vague. Unlike Darwinian selection, zygotic selection does not specify the direction of further evolution. It only gives a chance to continue existence of a mutation in an ontogene. The direction will be specified by the trends that exist in the living and thanks to which it emerged. They are currently unknown; however, the results of the relevant experiments define the address where the preserved mutation in ontogene will reside and where the next round of evolutionary events can occur. This address is the germline cells of the progeny carrying the mutation in ontogene within a permissive genotype.

Table 5 lists the results of an experiment on the effect of chromosomal rearrangements in the mother's

genome on the manifestation of the mutation in ontogene delivered from father. In the absence of rearrangement in mother, the mutation in ontogene kills all female progenies (column 2 shows the absence of daughters in cross). Chromosomal inversions *In*(2*LR*)*Cy, In*(2*LR*)*Pm,* and *In*(3*LR*)*D* in mother partially eliminate the dominant lethal effect of the mutation in ontogene so that daughters commence to appear in progeny (columns 4–5, 8–9, and 12–13). Noteworthy that the survived daughters contain not only the individuals with the *Cy, Pm,* and *D* inversions, but also those lacking these inversions. The observed effect of inversions can be validly regarded as a parental effect suggesting that the effect of inversions took place in the maternal germline cells during egg maturation. This experiment, as well as the others that demonstrate the parental effects in mutants, indicates that the most important events of an evolutionary scale are associated with the activity of ontogenes in germline cells.

Mutagenesis

The assertion that evolution is the process going on with the help of gene mutations prompts the idea that some mutations induce other mutations. This induction would allow a mutation to generate a set of mutations and, eventually, a new characteristic based on this set. However, geneticists have been constantly disappointed on this way. Any signs of chain mutagenesis have been undetectable. It is clear now that the absence of any induction of mutagenesis lies in the specificity of Mendelian genes. Usually, mutagenesis is tested according to the emergence of mutations in the parental germline. The Mendelian protein-coding genes are inactive, in the germline cells, making it senseless to expect an activation of mutagenesis there. The work with mutations in ontogenes immediately demonstrated the activity of this gene type in germline cells (parental effects) and the mutants in ontogenes displayed a very high rate of mutagenesis. Secondary mutations, morphoses, loss of dominant mutations, transposition of mobile level, and processing of lethality evidently confirm this. The epithet “explosive” [45, 46] precisely characterizes the mutagenesis observed in the mutants for ontogenes. It is not improbable that an increase in the basal metabolism in the mutants for ontogenes [9, 14, 43] is associated with the mutagenesis that continues in the soma.

Isolation

The isolation between two groups of organisms appears as the unfeasibility to have common progeny on the background of the fact that the production of progenies within each group is not disturbed. The relevant experiments show that a mutation in an ontogene is the first step in the formation of a *genetic isolate.* Once a mutation is formed in an ontogene, a single united panmictic population falls into two parts. The first part consists of the individuals lacking the mutation (say, *nonmutant subpopulation*). It is a continuation of the initial one and develops without any problems via panmictic reproduction. The second one consists of the progenies of the mutant for ontogene, which carry the mutation (correspondingly, *mutant subpopulation*).

The mutant subpopulation is *partially isolated* from the nonmutant subpopulation. This isolation appears as the death of part of common progeny of two subpopulations at the stage of zygote. However, the mutant subpopulation does not cease existing: part of the mutations survives by utilizing the suppressors of dominant lethality available in the initial population. Moreover, the mutant subpopulation commences to change because of the resulting genetic instability, which is induced by the presence of the mutation in ontogene. In the subsequent crosses of the representatives of both subpopulations, the composition of suppressors of dominant lethality can change qualitatively and quantitatively depending on the genetic variants emerging as a result of this genetic instability. The

mutant individuals can be with good reason regarded as a *mutant isolate.* They become the scene of a set of genetic alterations, which eventually can lead to a complete genetic incompatibility with the nonmutant part of population.

The phenomenon of mutation emergence in a Mendelian gene and its further fate in population have been considered in many papers on population genetics; however, the authors have not seen any reasons to regard the mutations in Mendelian genes as the cause of further isolation. This feature appeared in ontogenes and stems from their unique function, namely, the ability to organize the process of ontogenesis. The ability to form chains of genes is unalienable from the ability to break these chains. The ability to organize a control system simultaneously means the ability to destruct it or break it down. That is what mutations in ontogenes actually do.

Proteins play a decisive role in the vital activities of a living organism; correspondingly, this refers to the role of protein-coding genes as well. However, the latter *successfully function in both homozygous and heterozygous states* supporting panmixia and preventing emergence of nonuniformities in a genetic system. The emergence of a nonuniformity able to develop into separation of the initial genetic system into two subsystems incompatible with one another results from the specific feature of ontogenes, namely, their ability to act in homozygote and inability to act in heterozygote (lethality). It is no exaggeration to believe that it is the ontogenes with their ingenious features that determine the order of the living world in the form of isolated species.

Processing of manifestation of mutations in ontogenes

The research into ontogenes opens a new layer in the genetic phenomena associated with variation. In this case, the variation bears no resemblance to the classical mutagenesis in the form of changes in DNA stably inherited in the course of generations. Referring to Muller, Hadorn defines genetic mutation defines as «a change in genetic material that transforms its certain relatively stable state into another relatively stable state; the new state is reproduced in hundreds of thousands of cell generations" [47, p.24]. Unlike this (classical) pattern of mutagenesis, the mutations in ontogenes display a pattern of *chain mutagenesis,* in which an event of mutation in a gene does not end with the alteration of this gene but rather induces further instability of the overall genome, thereby producing secondary, tertiary, and so on mutations. In some parameters, this pattern resembles the so-called *epigenetic variation* but with an important amendment that *it refers to a particular group of genes, that is, ontogenes.* Some fragments of this variation in the form of the loss in lethal manifestation and homozygotization of dominant mutations are recorded and described, suggesting that variation in this case (1) develops in the course of the regular events taking place in genetic system; (2) follows a historically fine-tuned mechanism; and (3) most likely leads to two stable states of the genetic system, namely, a stable state preceding the period of variation ("old" norm) and a new stable state, that is, a new species.

Model of speciation

Thus, the following four processes the existence of which was unknown or vague when studying Mendelian protein-coding genes take place with involvement of ontogenes:

(1) *Editing of the program of individual development in germline cells of an individual.* Its material basis is two parental genomes. The program is edited in the germline concurrently with the development of morphogenesis in the somatic primordium. The players in this process are ontogenes;

(2) *Genetic instability* induced by a mutation in an ontogene. The instability appears at all developmental stages of a living organism but is especially important in germline cells because it leads to inherited changes;

(3) *Zygotic testing for compatibility of parental genomes.* The genomes that entered with the egg and sperm are compared. The genomes in the pronuclei interact at a distance. If they match, they fuse to continue the ontogenesis; otherwise, they fail to fuse and the zygote dies. The inference on the interaction of genomes follows from the parental effect of chromosomal rearrangement in the maternal genome on the lethality of the mutation in ontogene received from father [29, 32, 34]; and

(4) *Processing of ontogene manifestations.* The species-specific program of individual development can be changed by a regular activity of ontogenes. Homozygotization of the mutation in ontogene with elimination of dominant lethal and recessive lethal manifestations demonstrate that these changes are feasible.

These processes are regular and lead to the preservation and reproduction of the species-level program of individual development. However, once a mutation emerges in an ontogene, these processes commence to work on the creation of a developmental program distinct from the ancestral one. Thus, they work on speciation. The proposed model of speciation describes the events that, in our view, should follow the emergence of a mutation in ontogene. The model may be named *regeneration model. In general, this is the process of restoration of a species-level program of individual development disturbed by the mutation in ontogene.*

The overall process starts from a mutation in an ontogene in a germline cell. The appearance of mutation interferes with the *course of editing of the program of individual development.* However, the mutation interferes with the process but not arrests it. The gamete is formed and takes part in fertilization. The disturbance is brought to light in the zygote carrying two parental pronuclei. They fail to interact in a routine manner and do not fuse. Thus, the zygote dies without even starting to develop. In part of cases, the appropriate interaction of the parental genomes still takes place thanks to the variants existing in a partner genome, as well as the syngamy, so that the viable progeny carrying the "mutation + suppressor of dominant lethality" is formed. In the language of genetics, we referred to this situation as the "mutation in ontogene residing in a permissive genotype".

A favorable outcome combined (1) a partial isolation of mutant genome and (2) the permission for its further existence, including reproduction and secondary mutagenesis. Currently, it is not possible to specify the particular processes that take place in a persisting genome but we can assert that they do occur. This is suggested by both the changes in the energetics of mutants and the development of morphoses in progenies. Although morphoses are not inherited, their genetic nature is evident from the formation of groups of progenies with identical morphoses. Even the association of a defect with a particular side of the fly body is reproduced in the group of identical morphoses [27, 28, 39]. The facts described in Section 1.3 suggest a constantly ongoing alteration in the mutant genome.

The occurring changes can be regarded as the *regeneration of the species-level program of individual development.* The distinct trend of the removal of lethality in mutant stocks represents this particular *regeneration.* This commences from the elimination of dominant lethality followed by the removal of recessive lethality. The elimination of lethality indicates the ongoing regeneration. It forestalls an independent existence of a mutant clone on the background of the retained (and even deepening) isolation from the parental genotype. Individual facts of emerged sterile and later, fertile homozygotes demonstrate the progress in the regeneration of the program of individual development. In our earlier

work [44], we describe the arguments favoring the assumption that the program of species-level ontogenesis is tested in the direction from the last to first stages of ontogenesis, while this program in the soma is implemented in the opposite direction.

The homozygotization of a mutation in ontogene can be regarded as the next stage in speciation. Homozygotization marks the transition from the nascent program of individual development to a fully autonomous existence, comprising a complete isolation from the nonmutant subpopulation and a standard (homozygous) existence of ontogene in the genome. The assumption on homozygotization of mutation as a stage in the construction of "novel ontogenesis" agrees with the data on the natural polymorphism of drosophila populations.

The researchers adhering to the chromosomal theory of speciation report numerous cases of the correlation between speciation and the formation of chromosomal rearrangements in the genome [48–52]. Note that they mean not the rearrangements in a heterozygous state, which are most abundant in natural populations and, as a rule, lethal in homozygotes, but rather the particular chromosomal rearrangements in a homozygous state. This means that the regulatory system of ontogenesis is remodeled in the interval between the emergence of a rearrangement in a heterozygous state to its inclusion into the genome of a new species.

The meaning of the transition of a natural chromosomal rearrangement from a heterozygous to a homozygous state in the proposed model of speciation consists in the transition of the corresponding mutation in ontogene residing in the rearrangement into a homozygous state. This statement explains a well-defined type of correlation between speciation and the formation of a rearrangement. They do correlate but the degree of correlation is rather low. The low correlation results from their indirect relation. Speciation tightly depends on the ontogenes within the rearrangement rather than the rearrangement itself.

Other facts also suggest an indirect role of the chromosomal rearrangement in the course of speciation. The drosophila males carrying inversions in a heterozygous state display a decreased fertility. This appears as a high death rate of their progeny at the stage of zygote (white egg) as in the case with the mutations in ontogenes. The death is independent of the presence of inversion in the progeny [53]. Table 9 shows high death rates in the progeny of the drosophila males carrying inversions in their genome at the stage of white egg. The ratio of the classes "with inversion" to "without inversion" in the survived progeny is 1:1, thereby suggesting that the cause underlying the lethality of zygotes is not associated with the presence of a rearrangement there. The death is associated with the effect of the rearrangement on the function of the ontogenes in premeiosis [34]. Apparently, the events occurring with chromosomal rearrangements in experiment and in nature are readily explainable if we associate the mechanism of speciation with the mutations in ontogenes.

The elimination of lethality in the mutants for ontogenes requires a comprehensive study. The very first data demonstrate that this process differs from that occurring with the Mendelian genes. Although Mendelian genes are chemically akin to ontogenes, the latter function in a fundamentally different manner. Remote interaction independent of the mutual arrangement of nucleotide sequences in space [30] directly leads to the inference that this interaction is provided not chemically but rather physically via the formation of a physical field of an electromagnetic type. The state of compaction putatively characteristic of the active ontogenes perfectly agrees with the electromagnetic nature of interaction [29, 31].

The assumed biophysical way of activity is not the only one for ontogenes. We postulate that the

Table 9. Low fertility of the males carrying a chromosomal rearrangement [53]

Male genotype	Female genotype	Number of laid eggs	Number of resulting imagoes	Share of imagoes (imagoes/eggs)	Share of progenies with rearrangement of total number of progenies
In(2LR)lt^{m3}/ *pr pk cn*	*pr pk cn*	1987	1066	48.5 ± 5.4	0.45
In(2LR)bw^{v32g}/ *pr pk cn*	*pr pk cn*	1990	1599	80.7 ± 2.0	0.50
In(2LR)*B162*/ *pr pk cn*	*pr pk cn*	1405	538	40.5 ± 5.9	0.50
pr pk cn/*F*(2*L*); *F* (2*R*)*	*pr pk cn*	2195	1631	73.7 ± 3.0	0.50
	F(2*L*), *pr*; *C*(2*R*), *cn*	2286	145	12.6 ± 2.2	0.42
	C(2*L*), *b*; *F*(2*R*), +	2719	23	1.4 ± 1.0	0.52
	C(2*LR*)*EN*, *c bw*	2178	0	0.0	–
	Total			87.7	$x = 0.48$
In(2*R*)40/*F*(2*L*); *F* (2*R*)*	*pr pk cn*	2193	867	42.3 ± 10.0	0.51
	F(2*L*), *pr*; *C*(2*R*), *cn*	2325	22	2.0 ± 0.3	0.68
	C(2*L*), *b*; *F*(2*R*), +	2078	56	5.2 ± 0.6	0.52
	C(2*LR*)*EN*, *c bw*	2492	0	0	0
	Total			49.5	$x = 0.51$

* Yield of the viable progeny is determined as the sum of the numbers of imagoes in four crosses with different tester females [50].

activity of ontogenes in germline cells consists in the production of small nuclear RNAs [54]. Thus, ontogenes are most likely able to exert the activities of two types: biochemical activity with the help of small nuclear RNAs and biophysical activity with the help of wave action. The former is implemented in germline cells during editing of the program of individual development and the latter, while this program is deployed in the developing soma [32].

Zygotic selection is the process of self-development of genetic system, that is, the programmed response to an occurred damage in the system of individual development. The meaning of this response is the restoration of the coordinated work of genetic structures that guarantee the eventual construction of an actively functioning living organism. The restoration cannot be anything but the construction of an additional control structure supplementing the already existing ones. This is yet another increase in complexity performed according to the rules of the arrangement of the genetic system itself. Morphoses demonstrate which particular structure–function variants can be created. These are cellular ensembles [28]. This can be referred to as *the buildup of complexity.* As is shown above, this is a special evolutionary mechanism. The following specific mechanisms are necessary for this mechanism to exist: (1) genome editing; (2) “explosive mutagenesis”; (3) zygotic selection; (4) isolation; and (5)

processing of lethality.

Cooperation of Darwinian and zygotic selections in evolutionary process

Zygotic selection arranges a new model of individual development, *Bauplan,* and cellular ensemble for the future organism. However, this is not the entire program of individual development of an organism. To eventually develop into the organism, the cellular ensemble should be filled with proteins and energetically blend in with the ambient environment. The formed living system (an organism of a novel species) should be tested for its ability to exist under particular environmental conditions. Correspondingly, we assert that the selection of the fittest is obligatory and takes place concurrently with the zygotic selection. The material for the former is the mutations in Mendelian genes and the process itself is the famous Darwinian selection according to fitness. The zygotic selection and Darwinian selection act in cooperation.

However, note that the fact of zygotic selection changes the established view on the evolutionary process as the adaptation to habitat. The significance of Darwinian selection is not zeroed but rather considerably hypostatized. Correspondingly, the severe competitive relations between the adult organisms, which appear absolutely necessary in the case of the evolution that follows the Darwinian model, do not seem inevitable in this case. The genetic variants in the case of zygotic selection are rejected at the level of cells (zygotes) rather than adult organisms. That is why the general course of evolution looks more peaceful [24, 25] than it seemed earlier.

Conclusions

The discovery of a new class of genes (ontogenes) has emerged to be important not only for genetics, but also for the biology in general. Thanks to ontogenes, the biological phenomena, such as a high activity of germline cells, zygotic selection, and mechanism of biological isolation, came to light. The mutations in ontogenes (facultative dominant lethals) prove themselves as the structures able to perform mutually exclusive roles: the mutation of an ontogene in the presence of a lethality suppressor belongs to the species-level genome, whereas it does not belong to it (becomes a lethal) in the absence of suppressor. One and the same mutation acts as an isolating agent and as a germ for a novel species. The unique role of ontogenes in genetic system and the specificity in manifestation of their mutations suggest that ontogenes represent the material for evolution and the genetic tool for speciation. We named our model the regeneration model. The speciation there is represented as the process of regeneration of the genetic system damaged by the emergence of a mutation in an ontogene.

The proposed concept is fundamentally different from the Darwinian concept of speciation as “the inevitable result of the competition” for fitness. On the other hand, both concepts stem from the same root. Both consider the birth of a new species as the emergence and selection of the variants a living cell that once appeared but not as a result of repeated events when the living originates from the nonliving. In the Darwinian variant, this is the selection of mutations in Mendelian genes. The mutations are selected according to their phenotype among the adult breeder individuals. As for zygotic selection, this is the mutations in ontogene together with the suppressors of their lethal manifestation. The results of the cooperation between two types of selection are a new taxonomic unit (species) harmonized with the habitat.

The relations between organism and environment in our model differ from the Darwinian variant. According to Darwin, it is environment that controls the evolution of living beings, whereas the

evolution in the proposed model advances following the mechanism designed by the living itself and is already contained in the living. The model replicates the idea of autogenesis (orthogenesis or nomogenesis), repeatedly proposed earlier [55, 56]. Moreover, our model directly demonstrates that the activity of ontogenes in germline cells, zygotic selection, and isolation, so important for the progress of evolution, are the constituents of the very existence of a living organism (editing of the developmental program, fusion of genomes, creation of the unified developmental program, and so on). In other words, the structure and function of the living in our view are just a "screenshot" in the course of the evolution of living things. According to Dobzhansky, "nothing in biology makes sense except in the light of evolution" [57].

The most important result of our work is the experimental and theoretical elaboration of the idea that the implementation of the opportunities inherent in the DNA genetic machinery of the cell is the foundation for the evolutionary transformation of the living. The concept of the influence of environment on the evolutionary process, which strongly supported the general idea of evolution during its establishment, is not withdrawn from the agenda but cannot be regarded as the main driving force of evolution.

Acknowledgments

This research was supported by the Ministry of Science and Higher Education of the Russian Federation via the Institute of Cytology and Genetics, Siberian Branch, Russian Academy of Sciences (no. FWNR-2022-0015 on microdissection and FISH analysis). Microscopy was performed at the Core Facility for Microscopy of Biological Objects with the Institute of Cytology and Genetics, Siberian Branch, Russian Academy of Sciences (reg. no.3054), Russia.

References

1. Ch. Darwin, On the Origin of Species by Means of Natural Selection. Penguin Classics, 2019.
2. N.W.Timofeeff-Ressovsky, N.N. Vorontsov, A.V.Yablokov. An Outline of Evolutionary Concepts. Moscow: Nauka. 1969.
3. B. F. Chadov, Evolution as a phenomenon of the Universe formed: the strategy and tactics of the evolution of the living. Proceedings of the XXVIII Lubishev's Reading. Modern Problems of Evolution and Ecology. April 5-7, 2016. Ulyanovsk (Russia): UlGPU. P. 168-177.
4. E.V. Evdokimov, Evolution according to Spenser: Development of the hierarchy in the organization of matter by means of a stepwise integration and subsequent differentiation. Russ. J. Philos. Sci., 4(19) (2003): 64–83.
5. B.F. Chadov, E.V. Chadova, N.B Fedorova, Ontogenes and the Problem of Speciation. Journal of Evolutionary Science - 1(1) (2019): 33-47. DOI: 10.14302/issn.2689-4602.jes-18-2431.
6. B.F. Chadov, E.V. Chadova, S.A. Kopyl, N.B. Fedorova, A new class of mutations in Drosophila melanogaster, Dokl. Biol. Sci. 373 (2000): 423–426.
7. B.F. Chadov, Mutations in the regulatory genes in Drosophila melanogaster, in: Proc. Intern. Conf. Biodiversity and Dynamics of Ecosystems in North Eurasia, IC@G, Novosibirsk, August 21–26 (2000): 16–18.
8. B.F. Chadov, N.B. Fedorova, E.V. Chadova, E.A. Khotskina, Conditional mutations in Drosophila, J Life Sci. 5 (2011): 224-240.

9. B.F. Chadov, N.B. Fedorova, E.V. Chadova, Conditional mutations in Drosophila melanogaster: On the Occasion of the 150th Anniversary of G. Mendel's Report in Brünn, Mutat. Res. Rev. Mutat. Res. 765 (2015) 40–55, http://dx.doi.org/10.1016/j.mrrev.2015.06.001.
10. B.F. Chadov, Ontogenes in Drosophila melanogaster: genetic features and role in onto – and phylogeny, in: V.L. Korogodina, A. Chini and M. Durante (Eds), Modern Problems of Genetics, Radiobiology, Radioecology and Evolution, JINR, Dubna (2007) 80-91 (In Russian).
11. B.F. Chadov, Mutations capable of inducing speciation. In: V.N. Stegnij (Ed.) Evolution Biology. Tomsk State University Press, Tomsk, 1 (2001):138-162. http://www.evolbiol.ru/
12. B. F. Chadov, Facultative dominant lethals: genetics, ontogeny and phylogeny. In: V.N. Stegnij (Ed.) Evolution Biology. Vol. 2: Publishing Department Tom. State. Univ. (2002): 118-142. (In Russian). http://www.evolbiol.ru/
13. B. F. Chadov, Transformation of species and speciation - two forms of evolutionary transformation of the living. In: "The Evolution of Life on Earth" (ed. Podobina V.M.). 2005. Tomsk: Tomsk State University. P. 73-75. (in Russian).
14. B. F. Chadov, Fedorova N. B. Energetic destination of living and the evolutionary process. Proceedings of the international conference "Charles Darwin and modern science." 21-25 September 2009. St.-Petersburg. P. 235-237.
15. N. B. Fedorova, E. A. Khotskina, B. F. Chadov, Chromosomal rearrangements and speciation: explanation of the relationship between events. In: Genetics in XXI century: current state and prospects of development (Proceedings of the III Congress of the Vavilov Society of Geneticists and Breeders, Moscow, June 6-12, 2004). 2004. V.2. P. 274.
16. N. B. Fedorova, E. A. Khotskina, E. Ju. Mitrenina, B. F. Chadov, Chromosomal rearrangements and speciation: explanation of the relationship between events (in Russian). In: "Evolution Biology" (ed. V.N. Stegniy). Tomsk: Tomsk State University. 2005. V. 3. P. 107-120. (In Russian). http://www.evolbiol.ru/large_files/chadov2005.pdf.
17. B. F. Chadov, E. V. Chadova., E. A. Khotskina, N. B. Fedorova, Mutation in the ontogene – genome instability – appearance of new forms. In: "Evolution Biology" (ed. V.N. Stegniy). Tomsk: Tomsk State University. 2005. V. 3. P. 92-106. (In Russian). http://www.evolbiol.ru/large_files/chadov2005.pdf.
18. B.F. Chadov, E.V. Chadova, E.A. Khotskina, and N.B. Fedorova, Conditional lethal mutations shift the genome from stability to instability. Russ. J. Genet. 45 (2009) 276–286.
19. B.F. Chadov, <Gene-progene> quasicycle and evolution, In: L.E. Grinin, A.V. Markov, A.V. Korotaev (Eds.), Evolution: Problems and Discussions, LKI/URSS, Moscow, 2010, P. 280-301. (in Russian). DOI: 10.13140/2.1.4279.6324
20. B. F. Chadov, Natural selection: a way to produce new species or a permanent state of matter? Proceedings of the XXV Lyubischev's Reading. Modern Problems of Evolution. Ulyanovsk: UlGPU. 2011 P. 84-92.
21. B.F. Chadov, Cyclic Protomodel and phenomenon of evolution //Biocosmology- neo-Aristotelism, 3 (2013): 120-146. http://www.biocosmology.ru/.
22. B. F. Chadov, Evolution in the light of cyclic protomodel. Proceedings of the XXVIII Lubishev's Reading. Modern Problems of Evolution and Ecology. April 7-9, 2014. Ulyanovsk (Russia):

UlGPU. P. 56-64.

23. B. F. Chadov, Cyclic protomodel and the phenomenon of evolution. In: The anthology "Evolution: Megahistory and global evolution. The proceedings of the Symposium / Eds. L. E. Grinin, A.V. Korotayev. – Volgograd (Russia): Teacher, 2015. – P. 33-57. https://books.google.ru/books?isbn=5705745664
24. B.F. Chadov, E.V Chadova., N.B. Fedorova, Orthogenesis and Darwinism: Perspective of their synthesis in light of the conditional mutations data. Modern Problems of Evolution and Ecology. Proceedings of the XXX Lubishev's Reading. March 30--31, 2017. Ulyanovsk (Russia): UlGPU. P. 133-142.
25. B.F.Chadov, N.B. Fedorova, Zygotic selection in Drosophila melanogaster and a new edition of Darwin's concept of speciation. In: Evolution of Life on the Earth: Proceedings of the V International Symposium, November 12-16, 2018, Tomsk/Editor-in Chief V.M. Podobina - Tomsk: Publishing Hous of TSU, 2018. 49-51.
26. B.F. Chadov and N.B. Fedorova, Conditional Mutations and New Genes in Drosophila, In: M. Fasullo and A. Catala (Eds) Mutagenesis and Mitochondrial-Associated Pathologies (2020), http://dx.doi.org/10.5772/intechopen.103928
27. B.F. Chadov, and N.B. Fedorova, The Mutations Disturbing the Bilateral Symmetry in Drosophila, SCIOL Genet Sci. 2 (2019) 139-152.
28. B.F. Chadov, and N.B. Fedorova, Ontogenes and Their Role in Cellular Construction. Advances in Bioscience and Biotechnology, 14 (2023) 49-73. https://doi.org/10.4236/abb.2023.142004
29. N.B. Fedorova, B.F. Chadov, Gene interactions in Drosophila without contacts and chemical intermediaries, in: Abstracts Book of the International Conference on Cell and Experimental Biology (Virtual Conference), December 9-11, 2020, p. 6., https://cellexpbiol.unitedscientificgroup.org/proceedings/CEB- 2020_Abstracts.pdf>.
30. B.F. Chadov, N.B. Fedorova, Ontogenes and the paradox of homologous pairing, Advances in Bioscience and Biotechnology 12 (2021) 1-9, https://doi.org/ 10.4236/abb.2021.121001.
31. B.F. Chadov and N.B. Fedorova, Ontogenes and Chromosome Nondisjunction in the D. melanogaster Meiosis, Advances in Bioscience and Biotechnology 13 (2022): 317-335, https://doi.org/10.4236/abb.2022.138020
32. Chadov BF, Fedorova NB. New Class of Genes in D. melanogaster (Conditional Mutations, Ontogenes, and Biological Role of Ontogenes). Japan J Res., 4(6) (2023): 1-8. DOI: 10.33425/2690-8077.1079.
33. B.F.Chadov, E.V. Chadova, S.A. Kopyl, N.B. Fedorova, Delayed activation of the maternal genome during early development of Drosophila //Doklady Biological Sciences 01/2001; 378: 294 -8.
34. B.F. Chadov, E.V. Chadova, and N.B. Fedorova, A Novel Type of Gene Interaction in D. melanogaster, Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis 795 (2017) 27-30, https://doi.org/10.1016/j.mrfmmm.2017.01.002
35. B.F. Chadov, N.B. Fedorova, E.V. Chadova, Parental effects of conditional mutations and their explanations, Russ. J. Genet. 49 (2) (2013): 141-150, http://dx.doi.org/10.1134/S1022795413020038

36. B.F. Chadov, E.V. Chadova, N.B. Fedorova, The Genetics of Conditional Mutations and Individual Developmental Program in D. melanogaster. SCIOL Genet. Sci. 1 (2017): 3-21.
37. B.F. Chadov, E.V. Chadova, N.B. Fedorova, Conditional Mutations in Drosophila: Concept of Genes That Control Individual Development, Advances in Bioscience and Biotechnology 9 (2018): 243-272.
38. B.F. Chadov, E.V. Chadova, S.A. Kopyl, E.A. Khotskina, N.B. Fedorova, Genes controlling development: morphoses, phenocopies, dimorphs and other visible expressions of mutant genes, Russ. J. Genet. 40 (3) (2004): 271-281, http://dx.doi.org/10.1023/B%3ARUGE.0000021627.82588.41.
39. B.F. Chadov, E.V. Chadova, N.B. Fedorova, Epigenetic phenomenology in conditional mutants of Drosophila melanogaster: morphoses and modifications, in: S.M. Zakijan, S.M. Vlasov, E.V. Dement'eva (Eds.), Epigenetics, SD RAN, Novosibirsk (2012): 499–533 (In Russian).
40. B.F. Chadov, E.V. Chadova, N.B. Fedorova, Images of morphoses and modifications in Drosophila melanogaster conditional mutants, 2015, http://www.researchgate, http://dx.doi.org/10.13140/RG.2.1.2721.9042.
41. B.F.Chadov, N.B. Fedorova, Mutation in Ontogene and Emergence of Secondary Chromosome Damages in Drosophila Germline Cells. Advances in Bioscience and Biotechnology, 14(2023): 379-398. https://doi.org/10.4236/abb.2023.149025
42. N.B. Fedorova, and E.V. Chadova, Mutation in ontogene causes transposition of retrotransposon 412, In: V.A. Kunakh (Ed.), Factors of Experimental Evolution of Organisms, Logos, Kiev (2008): 210–215 (In Russian).
43. B.F. Chadov, N.B. Fedorova, E.V. Chadova, E.A. Khotskina, M.P. Moshkin, and D.V. Petrovski. Genetic Mutation Affects Energy Status of Drosophila, Russian J. Genet. 46 (9) (2010) 1062-1066, doi:10.1134/S102 2795410090127&sa_campaign=Email/ACE/OF.
44. B.F. Chadov, N.B.Fedorova, Ontogenes and of Individual Developmental Program in D. melanogaster. In: Advanced Research in Biological Science (2023) Vol. 6, Chapter 2. 8-39.
45. T.I. Gerasimova, L.J.Mizrokhi, G.P. Georgiev, Transposition burns in genetically unstable Drosophila melanogaster // Nature. 309 (1984): 714–716.
46. T.I. Gerasimova, "Transposition explosions" during genome destabilization in *Drosophila melanogaster.* In: "Molecular Mechanisms of Genetic Processes: Molecular Genetics, Evolution, and Molecular Genetic Foundations". Moscow: Nauka, 1985, pp. 13–20 [in Russian].
47. E. Hadorn, Developmental Genetics and lethal factors. London, N.Y., 1961.
48. Th. Dobzhansky, A.N. Sturtevant, Inversions in the chromosomes of Drosophila pseudoobscura. Genetics, 23 **(**1938): 28.
49. M. Ashburner, F. Lemeunier, Relationships within the *melanogaster* species subgroup of the genus *Drosophila (Sophophora)*. Inversion polymorphism in *D. melanogaster* and *D. simulans*. Proc. R. Soc. Lond. 193B (1976): 137-157.
50. F. Lemeunier, M. Ashburner, Studies on the evolution of the *melanogaster* species subgroup of the genus *Drosophila (Sophophora).* II. Phylogenetic relationsships of six species based upon polytene chromosome banding patterns. Proc. R. Soc. Lond. 193B (1976): 275-294.

51. F. Lemeunier, M. Ashburner, Relationships within the *melanogaster* species subgroup of the genus *Drosophila (Sophophora).* IV. The chromosomes of two new species. Chromosoma 89 (1984):343-351.
52. Th. Dobzhansky, Species after Darwin. In: “A Century of Darwin”. London – Toronto, (1969): 19-55.
53. B.F. Chadov, E.V. Chadova, E.A. Khotskina, E.V. Artemova, N.B. Fedorova, The main effect of chromosomal rearrangement is changing the action of regulatory genes, Russ. J. Genet. 40 (7) (2004) 723-731.
54. N.B. Fedorova, E.V. Chadova, and B.F. Chadov, Genes and Ontogenes in Drosophila: The Role of RNA Forms, Transcriptomics 4 (2016). p. 137.
55. I. Ju. Popov, Orthogenesis versus Darwinism. A Historical Scientific Analysis of the Concepts of Directional Evolution. St. Petersburg: Izd. St. Petersburg Univ., 2005 [in Russian].
56. I. Popov, Orthogenesis versus Darwinism. 2018. Springer Verlag. 209 p.
57. Th. Dobzhansky, Nothing in biology makes sense except in the light of evolution. The American Biology Teacher 35 (1973): 125–129.