

# Balinsky's Darwinian roots

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**Boris Ivan Balinsky (1905–1997) was Professor and Head of the Department of Zoology at the University of the Witwatersrand (Wits), Johannesburg, South Africa. He came to Wits in 1949 (via Munich and Edinburgh) from Kiev, where he was Professor of Embryology. As an acclaimed experimental embryologist he was especially famous for inducing a supernumerary limb in a newt when he was a 19-year-old student in Ivan Schmalhausen's laboratory in Kiev 1924. In Johannesburg he wrote his famous textbook of embryology, which influenced generations of students around the world. In addition to pioneering the application of electron microscopy to the study of early development, he tackled a variety of projects of general zoological interest. Lesser known is his latter day work, carried out during his retirement, on variation and heritability (especially of wing colouration) in the butterfly *Acraea horta*, on which he published five papers from 1974 to 1986. His butterfly work showing the loose connection between the genotype and phenotype, with the genotype expressing itself in a variable way in the face of a constant physical environment, is of special interest in the current era of evolutionary and ecological developmental biology. His exposure to the stimulating evolutionary ideas of Schmalhausen during his early Kiev years no doubt provided a context for his butterfly work. Some ideas about how the 'loose connection between the genotype and phenotype' may be achieved through behavioral modification or positional information during development are addressed in this paper in the light of recent work. In his eighties Balinsky worked on the classification of microlepidoptera on which he published several papers. He died in September 1997, just short of his 92nd birthday.**

**Key words:** Balinsky, butterfly, *Acraea*, wing-phenotype, heritability, Schmalhausen

## Background

Boris Balinsky was born in Kiev, Ukraine, in 1905—the year of the first Russian revolution. He was a student at the University of Kiev in the 1920s. His teacher, and later his mentor, was the luminary Ivan Schmalhausen (1884–1963). Schmalhausen was a vital force in the Russian development of the 'modern synthesis' in evolutionary biology<sup>1</sup> and is known for his book *Factors of Evolution: The Theory of Stabilizing Selection*.<sup>2</sup> While Balinsky absorbed the ideas of his teachers he fashioned his own career in experimental embryology, sparked by a paper he gave as a student on the determination of the germ layers<sup>3,4</sup> and especially by his remarkable experiment<sup>3</sup> in inducing a supernumerary limb in a newt when he was 19 years old.<sup>5</sup> He later went on to study endoderm development for which he was awarded the Kowalevsky Prize in 1940.<sup>3</sup> While experimental embryology was his main line of work, he was also a general zoologist and keen entomologist, collecting butterflies, stoneflies, and later dragonflies. Balinsky arrived at the University of the Witwatersrand (Wits) in 1949 at the age of 45, via Munich and Edinburgh (Waddington), having survived the turbulent events of 1917–1947 in Russia and Europe.<sup>3</sup> During his time at Wits he wrote his

famous textbook, *An Introduction to Embryology*,<sup>6</sup> which became a global classic, running to five editions from 1960<sup>6</sup> to 1981. He was also a pioneer in the application of electron microscopy for the study of early development. During his retirement, Balinsky turned to the study of variation and heritability in butterflies and published five papers from 1974 to 1986. His exposure during his early Kiev days to the vibrant holistic ideas in comparative embryology and evolutionary biology no doubt provided a context for this later work, as did his older-by-five-years contemporary from Kiev, Theodosius Dobzhansky.<sup>3</sup>

## Balinsky's evolutionary roots in the Kiev years

In 1968, Balinsky, as Professor of Zoology at the University of the Witwatersrand, wrote an article on Darwin for the Wits science students journal, *Probe*.<sup>7</sup> It seemed that he was merely doing his duty as Professor of Zoology, for we knew him not as an evolutionary biologist but as the celebrated experimental embryologist who had induced a supernumerary limb in a newt,<sup>5</sup> as well as for his famous textbook. I doubt any of us were aware of his unique evolutionary background and how it took root in the Kiev milieu of the 1920s and 1930s, spearheaded by the original thinking of Schmalhausen. Schmalhausen stood out in having mastered several fields related to problems of evolution, from comparative anatomy and comparative embryology to experimental embryology and growth.<sup>8</sup> However, from 1935, succeeding his teacher Severtsov, Schmalhausen was appointed Director of the USSR Academy of Science's Institute of Evolutionary Morphology in Moscow, as well as to the Chair of Darwinism at Moscow University. And for the next 15 years he focused on aspects of the theory of evolution,<sup>3,8</sup> as later set out in *Factors of Evolution*.<sup>2</sup> It was an original book that analysed the different forms of natural selection and the possible influence of these on the course of evolution.<sup>8</sup> As Gilbert<sup>9</sup> saw it, *Factors of Evolution* was 'nothing less than an attempt to integrate evolutionary morphology, population genetics, experimental embryology, and ecology into a coherent framework to provide a causal theory for evolution'. Rather accordingly, the field of interest of Schmalhausen's teacher Severtsov,<sup>8</sup> who preceded him in Kiev, was 'comparative anatomy and comparative embryology in their bearing on evolution'. For Severtsov, 'a complete theory of evolution must causally explain the morphological changes seen in palaeontology through the mechanisms of genetics, ecology, and embryology'.<sup>9–11</sup> When Schmalhausen accepted the directorship of the Moscow Institute of Evolutionary Morphology following Severtsov's death in 1935, he negotiated to maintain his Directorship in the Ukrainian Academy on a part-time basis and Balinsky, who in the meantime had been appointed as Professor of Embryology at Kiev University in 1933 at the age of 28, was appointed Deputy-Director of the Biological Institute in the Ukrainian Academy of Science.<sup>3,8</sup>

While Balinsky wrote about Schmalhausen's *Factors of Evolution* in his later years,<sup>8</sup> it is not clear when he first read the book. Schmalhausen records the development of his ideas from the beginning of 1938, when he was in Moscow. However, Balinsky's life in Kiev was at that time in a precarious state. During Stalin's purges in the 1930s, Balinsky's wife Katia was sentenced in 1937 to 10 years in a Gulag work camp (the sentence was later

reduced).<sup>3</sup> Then came the war with Germany from 1941 and Schmalhausen was evacuated from Moscow to Kazakstan,<sup>8</sup> all of which would have precluded Balinsky's access to him. Schmalhausen's manuscript was ready for publication at the end of 1943, with the Russian edition appearing in print after the war—in 1947—the very same year Balinsky moved to Edinburgh (see introductory remarks by Schmalhausen and Dobzhansky in *Factors of Evolution*<sup>2</sup>). The English edition of *Factors* was published in 1949, the year Balinsky sailed for South Africa. Against this dire background, a further disaster came with Lysenko's tirade in August 1948, in Leningrad, against the many supporters of Mendelian-based genetics, which resulted in their instant dismissal. Schmalhausen lost his position as Director of the Institute of Evolutionary Morphology and was expelled from Moscow University.<sup>8</sup> Following these traumatic times, Balinsky was no doubt cautious during his early years in South Africa about expressing an opinion on the history of these events. I never heard him talk, in the late 1950s or 1960s, about Schmalhausen's ideas on evolutionary biology. It was only later that I understood Balinsky's close involvement with, and his high and warm regard for, his mentor—especially after reading his 1980 retrospective on Schmalhausen<sup>8</sup> and his 1988 memoirs.<sup>3</sup>

As a student in Kiev in 1925, Balinsky attended Schmalhausen's lectures on evolution. Rather presciently for Balinsky's later career in South Africa (1949–1997), Schmalhausen stressed the importance of Raymond Dart's work in recognising the hominid character of *Australopithecus*—at the time that the idea still met with considerable scepticism.<sup>8</sup> It is also fascinating that Schmalhausen referred to the ideas of Holism, put forward by Jan Smuts<sup>12</sup> in 1926, which had some influence on his line of thinking, as in his 1938 book,<sup>13</sup> *The Organism as a Whole in Individual and Historical Development*. In 1936, Balinsky, who had a fair command of German, was asked by Schmalhausen to translate Anton Dohrn's famous book,<sup>14</sup> *The Origin of Vertebrates and the Principle of Succession (i.e., Change) of Functions*, from the original German into Russian. Dohrn was a strong advocate of Darwin's 'Theory of Evolution by Natural Selection'. Balinsky recalls that 'translating the book gave me great pleasure and also insight into some problems of evolution.' The translated book, with an introduction by Schmalhausen, was published in 1937.<sup>3,8</sup>

In his *Probe* article of 1968,<sup>7</sup> Balinsky noted that, 'one of the points of Darwin's theory, which turned out to be a somewhat weak one, was his understanding of variation and heredity'—and he went on to explain the changes of thinking following the characterisation of mutations, not known in Darwin's time. Balinsky was certainly interested in the nature of variation and heritability as a core problem in biology and was probably, at the time of writing the *Probe* article or even earlier, thinking about how he would address the problem. In a way it was inevitable that he chose to tackle the subject using butterflies. As an 11-year-old boy in the Ukraine, he was stimulated by Akasov's book on collecting butterflies as well as by Berge's *Small Atlas of Butterflies and Moths* during his summer visits to his grandfather's parish in the countryside and he became an avid collector and classifier for about ten years.<sup>3</sup> However, in looking for a less studied group of insects for collection and study, and hoping to make a contribution, he sought advice from Mr Theodosius (Theodore) Dobzhansky, who at the time was an assistant in the Zoology Department of the Agricultural Faculty of the Polytechnic Institute in Kiev. Dobzhansky suggested he study scale insects, which he himself had started some work on. They immediately went out into the grounds of the Polytechnic Institute and beat some bushes, but found nothing! After reading a book on *The Orthoptera and Pseudoneuroptera of the Russian*

*Empire* by Jacobson and Bianki, he was attracted to the orders which had aquatic larvae and he initially started working on mayflies from 1924. Then, for logistical reasons, he switched to stoneflies, especially on his summer trips to the Caucasus where they are abundant.<sup>3,15</sup> Subsequently, in South Africa, he focused on dragonflies. All this was undertaken in parallel with his embryological career and other broad zoological interests.

### Variation and heritability in butterflies

In anticipation of his formal retirement as Professor and Head of Department at Wits at the end of 1973, Balinsky prepared the way for his new line of research on variation and heritability in South African lepidoptera. In searching for a suitable species, he chose the African garden butterfly *Acraea horta*, which had the advantage of the caterpillars feeding on leaves of the tree *Kiggelaria Africana*, which he was able to grow in his garden. He also built himself a butterfly breeding shed and his study became a research laboratory. The whole operation was a going concern prior to his formal retirement. In his new role as an Honorary Professorial Research Fellow, and working from home, he was able to rear *Acraea horta*, starting with single pairs, through ten generations under conditions of inbreeding, mostly brother–sister matings.<sup>16</sup> He went on to investigate the inheritance of wing colour and wing spotting, as well as attempting to generate mutations by irradiation with X-rays and UV<sup>17–20</sup> (see Fig. 1).

Of special interest is his paper on the inheritance of wing colouration in females.<sup>17</sup> Male wing colour is brick-red. Female wing colouration ranges from red through orange to yellow, depending on the state of oxidation-reduction of the pigment xanthommatin, which is yellow in the oxidised form and red in the reduced form. Furthermore, by breeding and crossing of strains, he concluded that the condition is controlled by one pair of autosomal genes with expression in the female. In order to treat his results statistically, he classified wing colour into six classes.

The results showed that the genotype does not strictly determine the phenotype of the individual female, i.e. with the same geno-

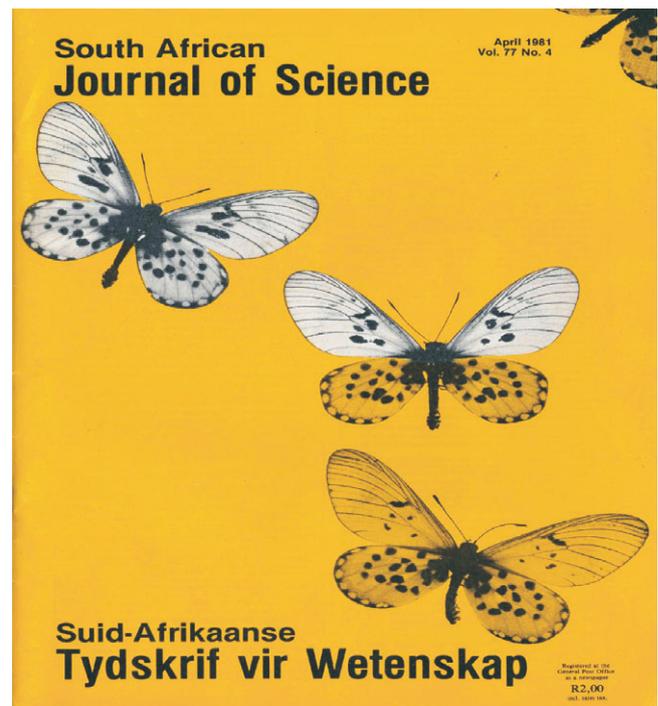


Fig. 1. Marginal spot patterning on the hindwings of *Acraea horta* investigated using X-ray irradiation, from Balinsky. The cover of *S. Afr. J. Sci.* 77 (1981).<sup>19</sup>

type the colour could vary within a wide range from pale yellow to bright red. Thus, yellow females could give rise to orange and brick-red females, red females to yellow and orange ones, and orange females to yellow and red ones. As he put it, with the expression of the genotype in individual females being highly variable, the selection differential of individual females has hardly any selection response. In a letter written to me on the 24 February 1977, he summarised the progress of his work as follows: 'What I think is really the main general result of the work I have done so far, is the loose connection in my butterflies between genotype and phenotype: the genotype expressing itself in a variable way... which of course is nothing new, known in *Drosophila*, but then *Drosophila* is only one species, and I am not sure that it can be considered as a 'typical' case of a wild animal'. While his findings showed that any particular female could give rise to progeny across the colour range of the inbred brood, a most intriguing aspect of the paper was that the averages of the colour classes of the parental generations were highly heritable in terms of filial generation averages.

Balinsky's finding that the genotype expressed itself in a variable way in his butterflies, is very much in line with Schmalhausen's 'reaction norm',<sup>2</sup> that is 'each genome encodes a continuous range of potential phenotypes and the environment each encounters determines its phenotype' (as phrased by Gilbert and Epel<sup>11</sup>). In Schmalhausen's words, 'every genotype is characterised by its own specific norm of reaction, which includes adaptive modifications of the organism to different environments'.<sup>2</sup>

While the influence of the environmental factors of temperature and light on butterfly wing colour has been well documented (see Gilbert and Epel<sup>11</sup>), Balinsky noted that the environment in his breeding experiments did not appear to be an influencing factor in determining the spectrum of colour polymorphisms within a brood, as each batch was treated in the same way under the same conditions. In the light of more recent knowledge, it is interesting to consider how the environment could influence wing colouration in the development of Balinsky's butterflies. Such a line of thinking is at the heart of the general pathway proposed by H.F. Nijhout<sup>11,21</sup> in which sensory information from the environment is transferred via the neuroendocrine system to the tissues where it is able to regulate gene expression. As summarised by Gilbert and Epel,<sup>11</sup> environmental signals (external or internal) are able to target neurosecretory cells in the brain, causing them to release prothoracicotropic hormone, which in turn stimulates the production of ecdysone by the prothoracic gland. Ecdysone enters tissues (inclusive of the imaginal discs<sup>11</sup>) where it is converted into its active form 20-hydroxyecdysone. Crucially, it turns out that the concentration of ecdysone, as single or multiple pulses, is key to its physiological function. At the molecular level, ecdysone, in the form of an active ecdysone-bound receptor complex, enters the nucleus and initiates gene expression at specific sites on the chromosome after recruiting histone acetyltransferase enzymes and other transcription factors.<sup>11</sup>

The involvement of the neuroendocrine pathway in wing colouration has been well documented<sup>11</sup> in the European map butterfly *Araschnia levan*, where the wing colouration at the time of eclosing from the pupal case is usually bright orange in spring and black in summer. The change of colouration, from spring to summer morphs, was found to be regulated by changes in day length and temperature during the larval period,<sup>11,22,23</sup> which suggested that a neuroendocrine signalling pathway is involved. It was further found that these environmental signals modulated the phenotype by regulating the amount of the hormone ecdysone during the larval stage of development.

Larvae that develop in spring do not experience a pulse of ecdysone, whereas summer larvae do. An injection of ecdysone converted the colouration of the spring form into the summer form. Most pertinently for the present discussion, the injection of intermediate amounts of ecdysone produced intermediate phenotypes not found in natural conditions.<sup>11,21</sup> As applied to Balinsky's butterflies, these findings suggest that the range of wing colouration in a brood could be underwritten by a range of ecdysone concentrations across the individuals of the brood. However, this still leaves open the question of how a range of ecdysone concentrations is established in a seemingly homogeneous batch kept under the same physical conditions, and how the range repeats in each generation.

### **'Each genome encodes a continuous range of potential phenotypes ... and the environment each encounters determines its phenotype'**

What type of mechanism could generate the range of wing-colour morphs in the brood from a single female in Balinsky's butterflies reared under the same physical conditions? As wing-colour pattern is determined in the late larval wing bud and the early pupal wing—in time for the synthesis of pigments shortly before the emergence of the adults<sup>24</sup>—one wonders if the graded colouring mechanism could be based on some sort of interactive process between caterpillars. This could relate to the amount of touching or amount of a secreted chemical which a caterpillar receives. The reception of such interactively generated signals may be assumed to follow a neuroendocrine routing such that the extent of stimulation a caterpillar receives would set its level of ecdysone. But how, with respect to Balinsky's results, would the average of the range of ecdysone levels in the parental brood repeat in the filial brood? Could the proposed interactions between the caterpillars, inhibitory or stimulatory, play out in a hierarchical cascade, which repeats in each generation? This remains an unanswered question. There is also a heterochronic aspect to the above sequence of events as wing pigments are synthesised in specialised wing scale cells in a fixed developmental succession, with the coloured pigments deposited first.<sup>25,26</sup> Hence the succession of scale development may determine the final wing colouration and is thus open to time-based modulation. This raises the question of the extent to which the level of ecdysone can influence the rate of developmental succession in the synthesis of wing pigments in the specialised wing scale cells. Does heterochronic modulation control wing colouration?

There is, however, another possible way in which a graded bias could be applied to developing embryos. It is based on the embryological principle<sup>27</sup> of positional information, or of gradients, that organise pattern formation. For example, with respect to *Acraea* butterflies, the eggs are laid in batches of typically 100–150 and are not scattered singly, as in most *Rhopalocera*. This opens up the possibility of establishing an inside–outside positional effect or gradient across the egg-batch. Eggs would take on a bias as a result of their position in the batch. Along the same general line of reasoning, a developmental bias could be imposed on eggs at an even earlier stage as a result of the spatial distribution of ovarioles in the ovary and the ensuing order of egg laying. In the contemporary context, such positional biasing could be effected by epigenetic changes in the DNA, such as in the level of cytosine methylation, chromatin packaging via histone variants, or in the binding of short antisense RNAs. A relevant aspect of the epigenetic circuitry is its regulatory effect on transcription, thereby positioning epigenetic reactions as possible regulatory switches acting on specific genes early on in

development, even from the time of oogenesis. In this way, epigenetic changes in the egg could, for example, affect specific genes that are later transcribed in the pathway of wing colouration, or which affect the rate of development of the neuroendocrine pathway and its secretory activity (a heterochronic effect).

It would be intriguing to assay epigenetic changes that occur in eggs from early developmental stages, especially with respect to Balinsky's findings—are there epigenetic differences between inside and outside eggs within a batch? A simple first experiment to address the above considerations, behavioural or positional, would be to follow the development of single eggs or embryos in isolation, with respect to the development of wing colouration.

### A concealed pool of genetic variability?

In his paper on the 'Variation and Inheritance of Wing Spotting in *Acraea*',<sup>18</sup> Balinsky was especially interested in the potential existence of a concealed pool of genetic variability, which in line with 'Neo-Darwinian concepts of evolution by natural selection ... may be made use of under changed environmental circumstances'. Assuming that such concealed variability was present in the form of recessive genes in a heterozygous state, he carried out breeding experiments but was not able to reveal this genetic reserve, even though '51 strains derived from the wild (were) inbred by brother-sister mating for a variable number of generations'.

In order to increase the amount of heritable variability in the study, Balinsky irradiated the pupae with X-rays and subsequently with UV. In one spotting variation following X-ray irradiation, there was a spectacular change in the shape of the wing marginal spots which were converted into longitudinal streaks.<sup>19,20</sup> However, although he experimented with different doses of radiation, the initial aim of the experiment—to obtain new mutant breeding strains for subsequent genetic study—was not achieved. He suggested this was possibly due to the limited scale of the operation, which was not large enough to produce recessive mutations.

While it is recognised that widespread genetic variation exists that may be unexpressed, it is only beginning to be appreciated that some of this cryptic variance may be important in maintaining phenotypic stability<sup>28</sup> and may thus play a role in keeping the developmental trajectory on track. It is this regulatory circuitry that has been deemed as a potential target in the modulation of the phenotype in the course of evolution. Such a line of thinking was central to Schmalhausen's analysis of the evolutionary process. His core idea hinged on 'the importance of the stabilisation of morphogenesis and the role of stabilizing selection in the process'<sup>2</sup>—an idea that went hand in hand with his concept of the autonomisation of development. Autonomisation of development is underpinned by the evolution of complex regulating systems under the influence of stabilising selection<sup>2,29,\*</sup>.

Understanding the nature and role of concealed variation has attracted a lot of interest in recent years. As Gibson and Dworkin<sup>32</sup> aptly put it, 'Cryptic genetic variation is the dark matter of biology.' Balinsky was clearly fishing in the right place. He would have been delighted by the relatively recent demonstration of Rutherford and Lindquist<sup>11,33</sup>—a year after he died—of a molecular mechanism which unmasks cryptic genetic variation through stress. This was achieved by mutating the heat shock gene *Hsp83*, thereby inactivating its protein Hsp90, which produced a range of 'concealed' phenotypes. The mechanism



Fig. 2. Balinsky in his eighties. (Photograph courtesy of his daughter, Helen David.)

hinges on the functioning of Hsp as a molecular chaperone that keeps many proteins in their functional 3D conformation.<sup>11,33</sup> Rutherford and Lindquist's inspirational conclusion was that Hsp90 functions as a capacitor for morphological evolution.

Balinsky published five papers on his butterfly breeding experiments, working from home during the first twelve years of his retirement (1974–1986) from the age of 69 until 81. It was as if he had waited for his retirement days to address this central biological problem (Fig. 2).

### Taxonomic studies

After the butterfly work, Balinsky, now in his eighties (Fig. 2), returned to his evergreen interest in taxonomy and chose to work on the identification of moths (microlepidoptera) from a vast collection housed in the Transvaal Museum. He published five articles on this work from 1987 to 1994,<sup>34–38</sup> by which time he was 89. As is well known, an important tool in the classification of the lepidoptera is the structure of the intricate parts making up the genitalia. It is held that 'male and female genital compatibility serves to isolate different species reproductively', and hence the notion of a lock-and-key hypothesis of genital evolution.<sup>39</sup>

On a visit to Balinsky's home in about 1990, he eagerly showed me the technique he used to prepare the specimens and we viewed the dissected genitalia under the microscope. When I naively suggested, knowing abysmally little about the field at the time, that the work informed on the emerging evo-devo approach—given that the intricate structures were at the crossroad of embryonic development, variation and selection—he was somewhat amused. Having spent a lifetime identifying insects, he had no doubt reflected on the changes and implications of these mating structures during evolutionary time. But more to the point, the immediate problem before him, now in his 80s, was the identification of microlepidoptera specimens in the museum collection—a feasible and remarkable, well-chosen project for his time of life. And then there was the exciting possibility of identifying some new species. But no doubt his benignly amused response also stemmed from his years of experience

\*It is intriguing that in the late 1930s and early 1940s, Waddington and Schmalhausen were both following a remarkably parallel line of thought, unbeknown to both at the time. Whereas Waddington's ideas were formulated as the canalisation (buffering) of developmental pathways and the idea of genetic assimilation, Schmalhausen wrote about the elimination of the perceptible deviations from the norm-of-reaction pathways as a result of natural selection and introduced his concept of 'stabilising selection'.<sup>29–31</sup>

which allowed him to view all this new 'evo-devo' talk as being rather 'old hat' – just a reawakening of the earlier Severtsov-Schmalhausen milieu at a molecular level. As he liked to remind one, fashions in research come and go, but are profitably reinvestigated with the tools of the time, as with his own swift application of the then new technique of electron microscopy to the study of early development. As succinctly expressed by Weaver and Hogan,<sup>40</sup> 'In developmental biology, as in all scientific fields, conceptual advances are tightly coupled to technological innovation'. Balinsky died at home on 1 September 1997, nine days before his 92nd birthday.

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