Evolocus

Article

Nomogenesis and the logic of chance

Dmitri L. Vyssotski[1,2,3]

Evolution of available genomes was shown to be proceeding through random changes, the changes that comprise the main modus of evolution (Koonin, 2011)[1]. Morphological evolution of available and extinct *Metazoa* was shown to be going on the basis of law, by means of precession of characters, where characters originally manifested in the young along in the course of time and evolution were displayed also in adult descendants (or supposed descendants) of that organism (Berg, 1922)[2]. This contradiction is obviously solved in nature, where the appearance of any new genetic locus in the genome and its further expression in the phenotype can be separated by unlimited period of time and by unlimited number of generations. The management of dormant genetic loci has come from the previous evolutionary stage, unimaginable today, where organisms were open systems with respect to the flow of genetic elements and were collecting, discriminating and storing genetic elements from the external environment. This was an important period when multiple systems for blocking and unblocking of genetic loci came into being. However even before this stage, it was even more fantastic evolutionary period where replication, transcription and translation were absent and Eigen cycle was not possible, but organisms were collecting randomly available components (proteins, RNA and DNA) by means of action acceptors (Anokhin, 1955)[3,4] – sites of double-stranded DNA mechanically compatible with useful components. Action acceptors themselves were unable to be replicated by modern way (no DNA polymerase!), but they were collecting their pseudo-copies from the environment – the pieces of DNA that were born in the environment and occurred to be compatible by chance with current action acceptors. Action acceptors, – the structures that sense presumably useful results or substances, were directing evolution from the early beginning and they are directing it today through activation and deactivation of dormant genetic loci.

In animals like mice, rats and guinea pigs, and also in humans (holocaust survivors and their progeny)[5], the phenomenon of phenotypic inversion can be observed[6-15]. Phenotypic inversion is defined as the opposite quantitative changes in untreated offspring with respect to treated, *e.g.* drug-treated, parents[11]. Phenotypic inversion was also reported in plants[16] and insects[17]. The term was introduced in 2004[18] and it is in use in connection with transgenerational epigenetic compensation[10-15,19-21].

In humans[5] and guinea pigs[15] the phenomenon of phenotypic inversion was registered also in methylation of DNA. Thus, the demethylation of 5-methylcytosine behaves here as a phenotypic trait and not as a heritable basis of transgenerational effects. Very often phenotypic inversion was obtained as a result of paternal drug treatment (prenatal, neonatal and adolescent), using such drugs as morphine[8-14], thyroxine[6,7,10-14] or complex substances like plastic mixtures[22]. However less often it was reported that phenotypic inversion can be expressed during lifespan of a given descendant in a semi-stochastic "all-or-none" fashion[14] (as "unstable, destabilized"[23]).

An example of such "all-or-nothing" expression of phenotypic inversion is shown in the **Fig. 1**, where randomly enhanced water consumption is recorded in female guinea pig, obtained from

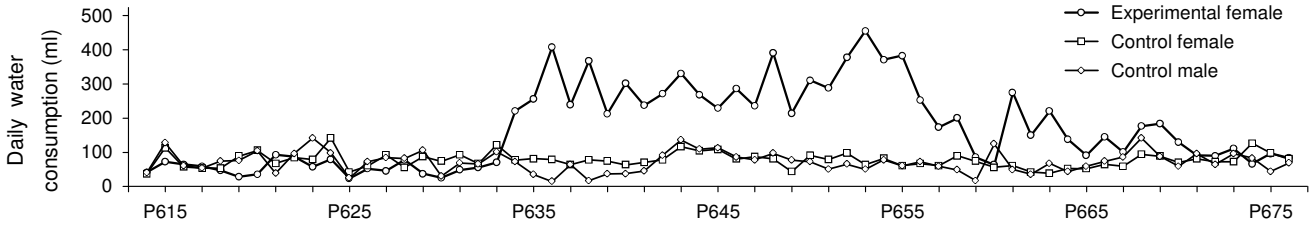

Figure 1 | Randomly expressed increased water consumption in the experimental female guinea pig, obtained from female with low adult water consumption and normal male. Postnatal days P614-P676 are shown. The stochastically increased water consumption in this female is in contradiction with the phenotype of her mother. Her mother was born in a litter of four, among normal littermates. The mother had decreased water consumption and increased locomotor activity and curiosity in home cage, observed during childhood, adolescence, adult life, and during pregnancy and lactation also.

[1]Evolocus LLC, Tarrytown, New York, USA. [2]Institute of Anatomy, University of Zurich, Zurich, Switzerland. [3]P.K. Anokhin Institute of Normal Physiology, Russian Academy of Medical Sciences, Moscow, Russia. Correspondence should be addressed to D.L.V. (vyssotski@evolocus.com).

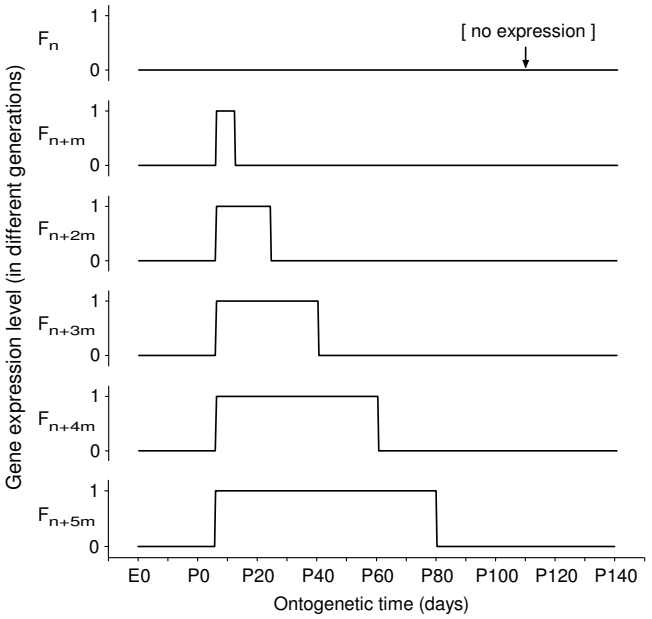

Figure 2 | Expression of one previously dormant genetic locus. Leo S. Berg has described the "precession of characters" in 1922: "… latent characters (factors, *genes*) originally manifested in the young alone… in the course of time and evolution are displayed also in the adult descendants (or supposed descendants) of that organism" [p. 75[2]; the word "*genes*" was italicized by Berg]. Ontogenetic time scale is shown for such animals as rats, keeping in mind experiments with methadone and morphine (Figs. 1[24] and 2[24], Supplementary Fig. 5a[11]). E0 – the first embryonic day, P0 – the first postnatal day.

female with unusually low water consumption. Note the random character of the expression of this phenotypic inversion (see also **Supplementary Figs. 2-3**). Of course, phenotypic inversion is supposed to be a result of compensatory changes[11]. Phenotypic inversion was also registered as an enhanced sensitivity to morphine in the F_2 progeny of chronically morphine-treated male Wistar rats, shown in the **Supplementary Figs. 4-7**. The relative lack of such observations in literature is a consequence of the absence of long-term records (it is thought to be difficult or impractical to monitor all descendants during their lifespan). Such records do exist for daily water consumption in guinea pigs (500 days) and morphine analgesia in rats (25 time points distributed among 7 days). Where long-term records are available, random "all-or-nothing" expression of phenotypic inversion during lifespan of a single animal is usually obvious.

Leo S. Berg has shown that new morphological changes can appear in evolution on the basis of law – by means of the precession of characters (**Fig. 2**). The time scale of shown example is given for the disturbance of opiate system in rats. This relatively new example was not discussed by Berg. The appearance of any new morphological trait, described by Berg, is an "all-or-nothing" response that is non-controllable or poorly controllable in amplitude, but nicely regular in temporal dimension during both ontogenesis and phylogenesis.

In modern experiments with transgenic mice, schematically shown in the **Fig. 3**, the disappearance or attenuation of phenotype in successive generations was observed rather often, but it was not reported so often due to social pseudo-scientific reasons. Both the observations of Berg concerning the appearance of dormant traits in evolution and the modern observations concerning the disappearance of phenotype in successive generations of transgenic mice demonstrate that *Metazoa* have sufficient molecular tools to control dormant genetic loci and to use them purposively.

The evolution of biochemical syntheses, described by Norman H. Horowitz (1945)[25] (**Fig. 4**), implies that any chain of biochemical reactions was developing in evolution from its final result (product). And all further steps were growing from the right to the left (shown as sequence: ד ← ג ← ב ← א), where each new enzyme was introduced by purpose – to provide substrate for previously existing process. Thus, this chain as a whole was build up as a purposive structure, being strictly purposive during each step of its evolution. Each additional step was satisfying the pre-existing action acceptor – the structure that can sense the presence and can use the result of this newly added step. The whole schema of Horowitz is an example of evolution, determined by law, determined by the requirements of pre-existing functional systems.

The law of homologous series in variation, discovered by Nikolai I. Vavilov (1922)[26], also can be used as an illustration of evolution, determined by law. Usually, similar heritable deviations (variations) in different species are explained by mutations in similar important genes that are normally expressed. But if it would be so, such events would be very rare, because such changes would be recessive and observable only in homozygous samples. Contrary to this, similar variations are formed by suddenly expressed dormant genetic loci those are also similar between species. Their sudden expression produces detectable effect in heterozygous individuals, being obviously dominant. Here we would like to repeat that in the experiments with paternal drug treatment[6-14] mothers were always drug-naïve.

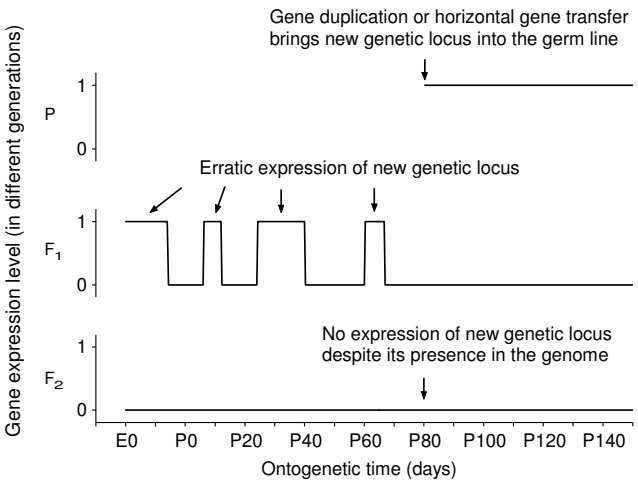

Figure 3 | New genetic locus is submerging into dormancy. In mammals, this process needs at least three shown generations (theoretically, in an idealized situation). In real life, 6-12 generations are required to bring new genetic locus into completely dormant state (many experiments with transgenic animals, mainly mice, are pointing out that this estimation is correct, at least for some genetic loci)[27,28]. Similar results, being frequently obtained, remain typically unpublished (nobody would like to report the disappearance of the phenotype discussed in the previous own article).

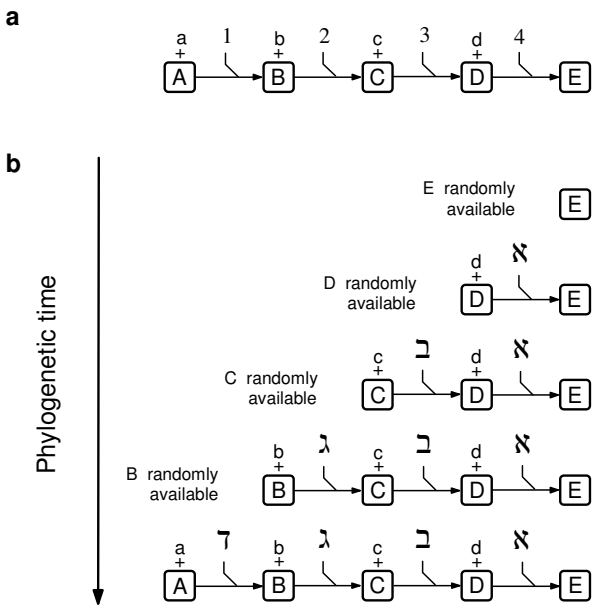

Figure 4 | The evolution of biochemical syntheses by Norman H. Horowitz (1945)[25]. **a**, Chain of biochemical reactions, shown schematically from substrate A to product E, is catalyzed by a set of specific enzymes 1, 2, 3, 4. **b**, In evolution, the order of appearance of specific enzymes is the opposite to the mentioned above and it can be shown as א, ב, ג, ד. Substance, known now as a product, at some point of evolution was randomly available from the environment. At the moment of its partial disappearance from the environment, but under condition that it still could be produced somehow from other available substances, its synthesis was beneficial and specific enzyme came into being.

So, we are dealing with dominant effects in the progeny – with expression of previously dormant genetic loci. Similar results (*i.e.* expression of previously dormant genetic loci) were obtained during domestication of silver foxes by Dmitry K. Belyaev[29,30]. Historically, homologous series of variation were first observed in wheat, which is usually self-fertilized, and later the same regularities were confirmed in rye, a typical cross-fertilized plant (p. 58)[26].

The term "action acceptor" was first introduced by Peter K. Anokhin in 1955[3,4] to describe behaviour of animals, at that time – dogs, as a brain-related feature. However the first action acceptors were present even before the appearance of replication, transcription and translation. Strictly speaking, the action acceptor is the first structure that appears in phylogenetic development of any functional system and this structure can sense and potentially use randomly appearing results, those are born in the external or internal environment by chance. All processes, even so complex as cell division, were appearing in evolution as random events. First – appearing purely by chance. Then – appearing with increased probability during some periods and appearing with decreased probability during some other periods of ontogenesis. Finally – appearing as clearly deterministic and well-controlled processes. Each time the action acceptor was formed before the next evolutionary step, and the next evolutionary step, like the next ferment in a biochemical chain, was found and raised up by the pre-existing action acceptor.

Typically our attention is focused upon the effector parts or production lines that produce "real result". If we see some feedback loop, we have a tendency to accept it as a relatively late addition that just slightly improves this system. However in real life, all feedbacks with their action acceptors were formed in evolution before all currently observable effector parts of given functional systems. It was an action acceptor that was the main acting agent in organization of all effector components from randomly available parts. Each of these parts could be first introduced at any previous evolutionary stage by chance.

Thus, from the early beginning the evolution was proceeding under control of very short and very strong feedback loops – internal feedback loops from the action acceptors. The shortest feedback loop was typically the strongest one. This type of evolution looks teleological and internally purposive. It is teleological and internally purposive – no secret here. For discussion of real teleology and pseudo-teleology of Darwinism we would like to refer to the book of Nikolai Ya. Danilevski,

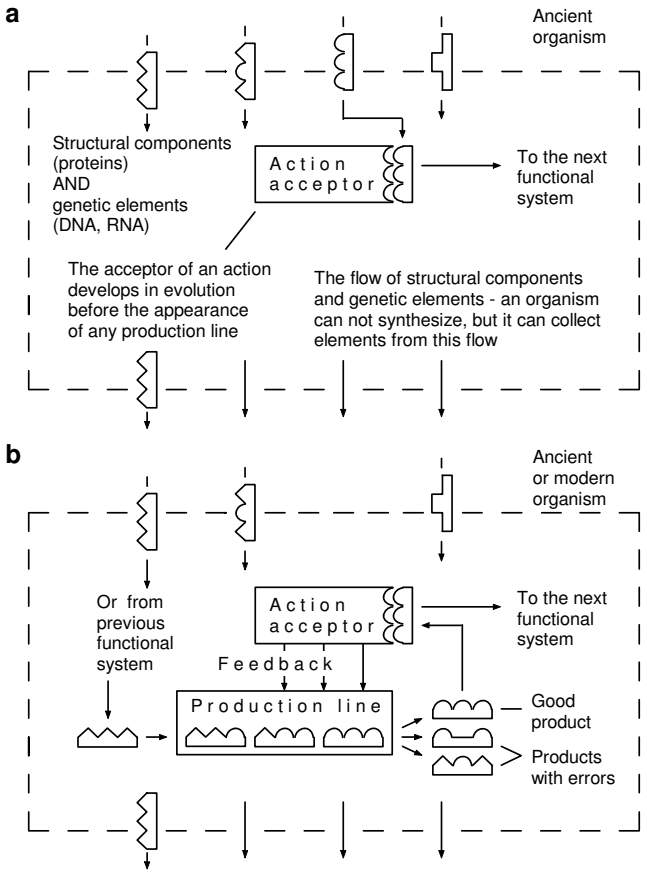

Figure 5 | Action acceptor in evolution. **a**, Early (ancient) organism was an open system not only in terms of energy, but in terms of its structural and genetic components also. It was not able to synthesize, but it was able to collect many components from the environment. The process of collection of components was performed by a set of action acceptors. **b**, Evolution of any production line starts from the acceptor of an action – from formation of potential feedback loop which appears in evolution before the first effector components of given functional system. Functional system is an entity that is searching for or is supporting the existence of some positive (useful) result with a help of feedback loop. The detector of useful result (action acceptor) is the first element in formation of feedback loop, see Fig. 6.11 (p. 241)[4] and Fig. 6.18 (p. 253)[4].

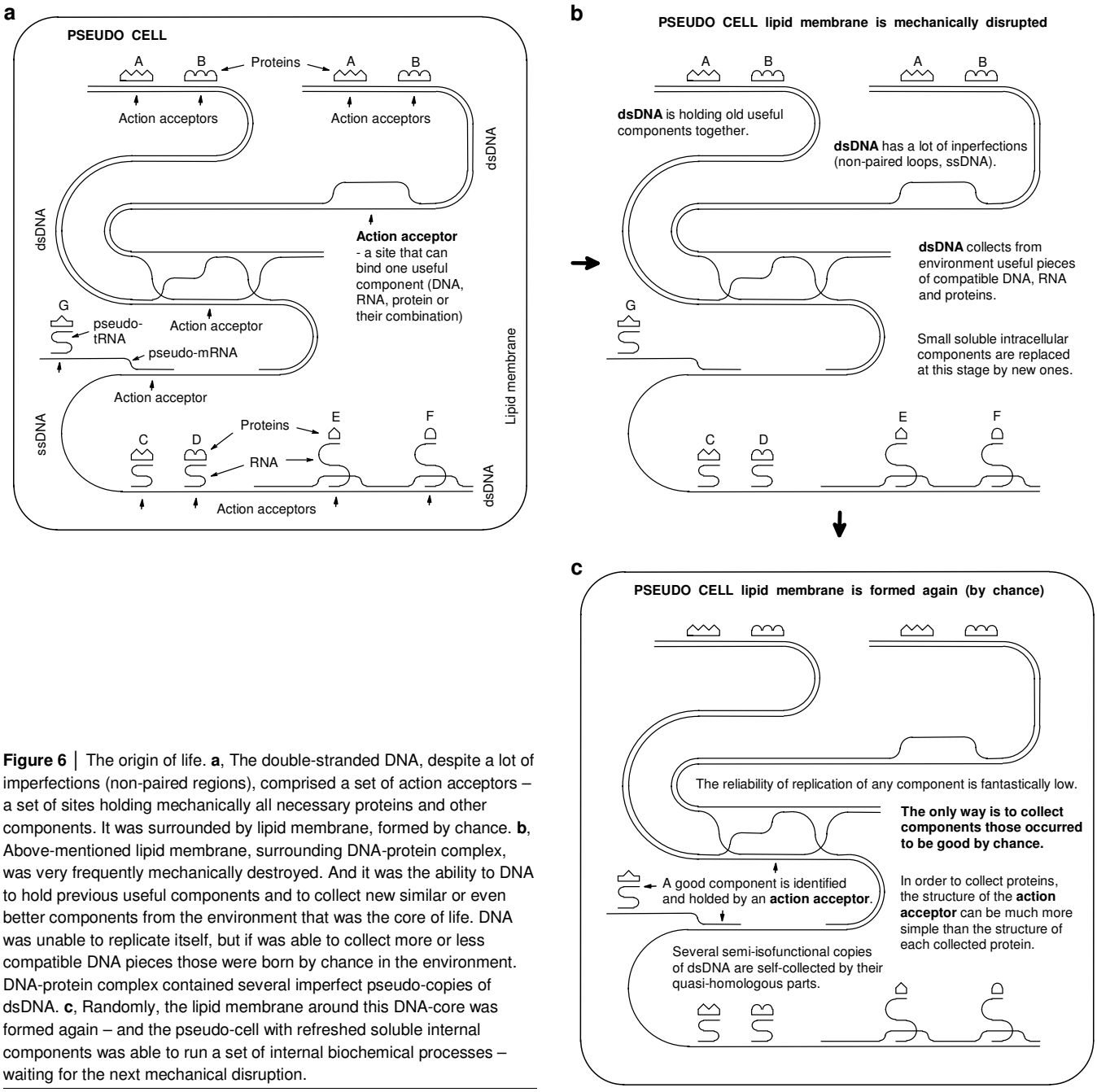

Figure 6 | The origin of life. **a**, The double-stranded DNA, despite a lot of imperfections (non-paired regions), comprised a set of action acceptors – a set of sites holding mechanically all necessary proteins and other components. It was surrounded by lipid membrane, formed by chance. **b**, Above-mentioned lipid membrane, surrounding DNA-protein complex, was very frequently mechanically destroyed. And it was the ability to DNA to hold previous useful components and to collect new similar or even better components from the environment that was the core of life. DNA was unable to replicate itself, but if was able to collect more or less compatible DNA pieces those were born by chance in the environment. DNA-protein complex contained several imperfect pseudo-copies of dsDNA. **c**, Randomly, the lipid membrane around this DNA-core was formed again – and the pseudo-cell with refreshed soluble internal components was able to run a set of internal biochemical processes – waiting for the next mechanical disruption.

published first in 1885[31-33], – it is fantastically important even today. As soon as functional system occurred to be equipped with even weak internal feedback loop – it has information about its own efficiency. And "efficiency" was determined in physiology by Alexander M. Ugolev[34,35] as relation of positive effects to negative ones ("cost factors"). It might be difficult to imagine "ideal organism", but we can always imagine "ideal functional system" – a system that is absent, but its positive result is achieved – this idea was first introduced by Genrich S. Altshuller[36] with respect to technical systems. The increase in complexity, observable in evolution, is not a purpose *per se*, but higher complexity is often, but not always, linked with higher efficiency. Parasitic organisms, evolving towards simplicity, are also good examples of the principle of efficiency.

Thus, any functional system of the organism has an ability, at least theoretically, to evolve towards "ideal functional system" and it can do so using its own internal feedback loops. It would be an error to assume that such feedback loops are good only for relatively simple optimization of the process. Any process exists usually under the pressure of contradictive forces and requirements. An attempt to increase one positive feature typically leads to decrease of another positive feature or to increase of some cost factor. Only the invention that can increase the main positive effect without the increase of the main cost factor would be really important evolutionary step, and this step will be done also with participation of local feedback loops, but the last remark does not mean that this step will be easy to perform.

As shown in the **Fig. 5**, the formation of an action acceptor and the formation of potential feedback loop are preceding in evolution the appearance of effector components of given functional system. The structure that senses the positive result develops in evolution first of all. At the beginning the result can be achieved only randomly – due to pure chance. The effector components will increase the probability of the appearance of positive result only later in evolution.

In modern organism, randomly available genetic and structural components are recruited by the action acceptor into production line in order to achieve qualitatively and quantitatively acceptable final result of this functional system. In modern organisms some action acceptors can be fantastically complex, distributed among multiple cells, but their main function remains the same – to search for and to support the desirable state of the organism or situation (not just to sense more or less good products among products with multiple errors). With respect to genetic components it was necessary not only to collect them, but to put them into domesticated state. The domesticated state means that the organism has an ability to switch given genetic element "on" and "off". The "on-off" switch – presumably reversible genetic change – has appeared in evolution even before the appearance of reliable replication. It means that an ancient organism was unable to reproduce incoming genetic elements, but it was able to switch them "on" and "off" in accordance with requirements of this organism.

As shown in the **Fig. 6**, the life on Earth has started when reliable replication, transcription and translation were absent (everything – below Eigen threshold[1,37]). Trans-membrane transport and trans-membrane potential were absent also. However, double-stranded DNA comprised the core of life. Its task was to collect and hold together all other necessary components (more or less similar DNA, more or less useful proteins and more or less useful RNA – all of them were randomly available from environment – they were developed by pure chance at the beginning of life). RNA was served as an intermediate factor in order to hold useful proteins that were not interacting with dsDNA sufficiently.

The mechanical disruption of this pseudo-cell was not only an analogue of cell division, but it was also an analogue of cell feeding. Whether the above-mentioned collection by dsDNA of more or less similar pieces of dsDNA together with other components could be described as "compositional inheritance as a mechanism of self-reproduction"[38] is an open question. At the beginning of life the mechanical disruption of pseudo-cell was really chance event. Only afterwards the pseudo-cell was able to increase probability of mechanical disruption at some stage of its existence and to decrease probability of mechanical disruption at some other stage of its existence.

Note that proteins that were binding to dsDNA directly, at the next stages of evolution will be "transcriptional factors". Replication, transcription and translation were developed under the control of action acceptors that were collecting only more or less successfully replicated, more or less successfully transcribed and more or less successfully translated components. Action acceptors were (and they remain!) the core elements of life that were able to compensate the fantastically low reliability of replication, the fantastically low reliability of transcription and the fantastically low reliability of translation. All three above-mentioned processes were developed under the control of very

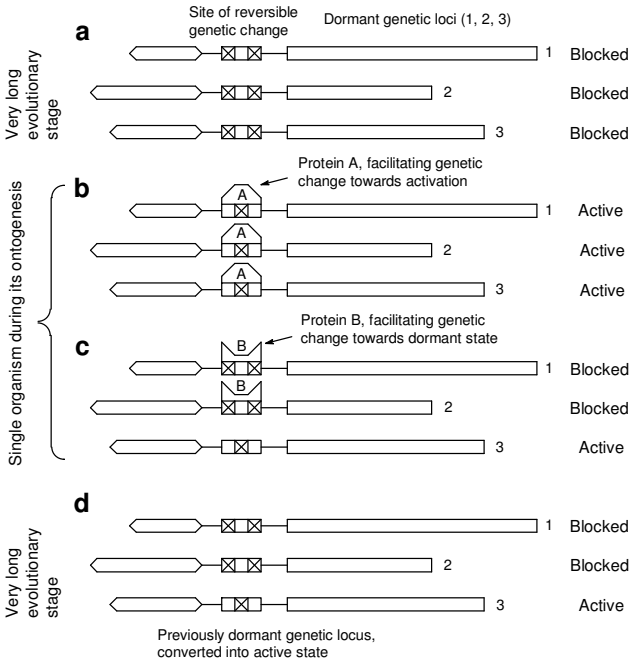

Figure 7 | Activation of previously dormant genetic locus in evolution. **a**, Three dormant genetic loci, each with reversible genetic change in the area of regulatory sites, are shown. **b**, In a deeply stressful situation the specific protein A is expressed, it binds to the site of reversible genetic change and increases the probability of its conversion into active state. **c**, In the exactly the same organism the protein B is expressed, it binds to the same site of reversible genetic change and increases the probability of its conversion into dormant state, but it can not do so with very highly expressed gene # 3. **d**, All previously expressed proteins A and B are finally disappeared, but previously dormant gene # 3 remains in active state (accessible for further regulation of its expression) forever. Similar process was called "orthoselection" in 1934 by J.W. Harms (Harms discussed the transition of vertebrate animals from water to land through multiple attempts, linked with transition of genes from "active" into "passive" state and *vice versa*)[39,40]. See **Supplementary Information**.

local, very short and very strong feedback loops. All proteins, facilitating necessary reactions, were collected together with products of the above-mentioned reactions by dsDNA, even despite any "knowledge" of their interactions were absent in the system (useful components should be held together – that is the principle). Very complex machinery of replication, transcription and translation was formed by means of collection of components that were formed independently and purely by chance. It means that DNA templates and proteins that were later formed of the basis of these templates, at the beginning of life were collected together just because the presence of templates is correlated with the appearance of above-mentioned proteins – both templates and proteins were formed at the beginning of life independently and mainly by chance.

As a short summary we can say that the evolution of the genome of any organism is always random – it is directed only by chance (Koonin, 2011)[1]. Morphological evolution and physiological evolution in general is always determined by law (Berg, 1922)[2]. And it was so even before the appearance of replication, transcription and translation. We can suppose that the very first action acceptors have appeared in evolution also by chance. As soon as the first action acceptors were present and

were able to collect from the environment useful components of different nature, randomly available (DNA, RNA, proteins), the first functional systems were formed and all further evolution was dictated by the requirements of the pre-existing functional systems. This process was and it is internally purposive, however some final goal is not absolutely necessary for its existence. It is sufficient to have local vector of development, each time based on local efficiency of currently present functional systems. This vector sometimes can be erroneous and it can lead to the extinction of the species, but it is always present (just because functional systems with their feedback loops are always present inside given organism).

Thus, evolution is a purposive process, and each its step is based on local efficiency. These are no analytical means that could distinguish between the results of the above-mentioned process and the results of evolution, directed by God, if our understanding of God is provided by Orthodox Judaism. In both cases all local decisions are solutions of contradictions between local positive effects and local cost factors. Thus, both descriptions have equal relation to the observable universe.

References

1. Koonin, E.V. *The Logic of Chance: The Nature and Origin of Biological Evolution* (FT Press, Upper Saddle River, New Jersey, 2012).
2. Berg, L.S. *Nomogenesis or Evolution Determined by Law* (MIT Press, Cambridge, 1969).
3. Anokhin, P.K. New data on the characteristics of the afferent mechanism of the conditioned reflex and their significance for psychology. *Problems of Psychology* (6): 16-38 (1955) [Publ. in Russian: Анохин П. К. Новые данные об особенностях афферентного аппарата условного рефлекса и их значение для психологии. *Вопр. психол.*, 1955, № 6, стр. 16-38].
4. Anokhin, P.K. *Biology and Neurophysiology of the Conditioned Reflex and its Role in Adaptive Behavior* (Pergamon Press, NY, 1974).
5. Yehuda, R., Daskalakis, N.P., Bierer, L.M., Bader, H.N., Klengel, T., Holsboer, F. & Binder, E.B. Holocaust exposure induced intergenerational effects on FKBP5 methylation. *Biol. Psychiatry* 2015 Aug 12. doi: 10.1016/j.biopsych.2015.08.005.
6. Bakke, J.L., Lawrence, N.L., Bennett, J. & Robinson, S. Endocrine syndrome produced by neonatal hyperthyroidism, hypothyroidism, or altered nutrition and effects seen in untreated progeny. In *Perinatal Thyroid Physiology and Disease*, Fisher, D.A. & Burrow, G.H., Eds. (Raven Press, New York, 1975), pp. 79-116.
7. Bakke, J.L., Lawrence, N.L., Robinson, S. & Bennett, J. Observations on the untreated progeny of hypothyroid male rats. *Metabolism* **25**, 437-444 (1976).
8. Eriksson, P.S., Ronnback, L. & Hansson, E. Do persistent morphine effects involve interactions with the genome? *Drug Alcohol Depend.* **24**, 39-43 (1989).
9. Cicero, T.J., Nock, B., O'Connor, L., Adams, M.L. & Meyer, E.R. Adverse effects of paternal opiate exposure on offspring development and sensitivity to morphine-induced analgesia. *J. Pharmacol. Exp. Ther.* **273**, 386-392 (1995).
10. Vyssotski, D.L. *Transgenerational Epigenetic Compensation of Paternal Drug Treatment. Supporting Online Material* (Evolocus, New York, 2010). www.evolocus.com/publications/vyssotski2010som.pdf
11. Vyssotski, D.L. Transgenerational epigenetic compensation: Heritable compensation of disturbed functionality. *Evolocus* **1**, 1-6 (2011).
12. Vyssotski, D.L. Transgenerational epigenetic compensation in evolution. *Evolocus* **1**, 7-12 (2012).
13. Vyssotski, D.L. Transgenerational epigenetic compensation and sexual dimorphism. *Evolocus* **1**, 13-18 (2013).
14. Vyssotski, D.L. Transgenerational epigenetic compensation and natural selection. *Evolocus* **1**, 19-24 (2014).
15. Weyrich, A., Lenz, D., Jeschek, M., Chung, T.H., Rübensam, K., Göritz, F., Jewgenow, K. & Fickel, J. Paternal intergenerational epigenetic response to heat exposure in male Wild guinea pigs. *Mol. Ecol.* **25**, 1729-1740 (2016).
16. Durrant, A. The environmental induction of heritable change in *Linum*. *Heredity* **17**, 27-61 (1962).
17. Vuillaume, M. & Berkaloff, A. LSD treatment of *Pieris brassicae* and consequences on the progeny. *Nature* **251**, 314-315 (1974).
18. Vyssotski, D.L. *Elements of Biological Concepts* (Nauka, Novosibirsk, 2004) [Publ. in Russian: Высоцкий Д.Л. *Элементы биологических концепций* (Наука, Новосибирск, 2004)]. www.evolocus.com/publications/vyssotski2004.pdf
19. Guerrero-Bosagna, C. & Skinner, M.K. Environmentally induced epigenetic transgenerational inheritance of phenotype and disease. *Mol. Cell. Endocrinol.* **354**, 3-8 (2012).
20. Crews, D. & Gore, A.C. Epigenetic synthesis: a need for a new paradigm for evolution in a contaminated world. *F1000 Biol. Rep.* **4**, 18 (2012).
21. Jablonka, E & Lamb, M.J. *Evolution in Four Dimensions: Genetic, Epigenetic, Behavioral, and Symbolic Variation in the History of Life*, revised edition (MIT Press, Cambridge, 2014).
22. Manikkam, M., Guerrero-Bosagna, C., Tracey, R., Haque, M.M. & Skinner, M.K. Transgenerational actions of environmental compounds on reproductive disease and identification of epigenetic biomarkers of ancestral exposures. *PLoS One* **7**(2), e31901 (2012).
23. Lysenko, T.D. *Agrobiology: Essays on Problems of Genetics, Plant Breeding and Seed Growing* (Foreign Languages Publishing House, Moscow, 1954).
24. Smith, D.J. & Joffe, J.M. Increased neonatal mortality in offspring of male rats treated with methadone or morphine before mating. *Nature* **253**, 202-203 (1975).
25. Horowitz, N.H. On the evolution of biochemical syntheses. *Proc. Natl. Acad. Sci. USA* **31**, 153-157 (1945).
26. Vavilov, N.I. The law of homologous series in variation. *J. Genet.* **12**(1), 47-89 (1922).
27. Crabbe, J.C., Wahlsten, D. & Dudek, B.C. Genetics of mouse behaviour: Interactions with laboratory environment. *Science* **284**, 1670-1672 (1999).
28. Phillips, T.J., Hen, R. & Crabbe, J.C. Complications associated with genetic background effects in research using knockout mice. *Psychopharmacol.* **147**, 5-7 (1999).
29. Belyaev, D.K. Destabilizing selection as a factor in domestication. *J. Hered.* **70**, 301-308 (1979).
30. Belyaev, D.K., Ruvinsky, A.O. & Trut, L.N. Inherited activation-inactivation of the *star* gene in foxes. *J. Hered.* **72**, 267-274 (1981).
31. Danilevski, N.Ya. *Darwinism: A Critical Study*. Vol. 1, Part 1 (M.E. Komarov, St. Petersburg, 1885) [Publ. in Russian: Данилевский Н.Я. *Дарвинизм: Критическое исследование*. Том 1, Часть 1 (Издание М.Е. Комарова, С.-Петербург, 1885)].
32. Danilevski, N.Ya. *Darwinism: A Critical Study*. Vol. 1, Part 2 (M.E. Komarov, St. Petersburg, 1885) [Publ. in Russian: Данилевский Н.Я. *Дарвинизм: Критическое исследование*. Том 1, Часть 2 (Издание М.Е. Комарова, С.-Петербург, 1885)].
33. Danilevski, N.Ya. *Darwinism: A Critical Study*. Vol. 2 (M.E. Komarov, St. Petersburg, 1889) [Publ. in Russian: Данилевский Н.Я. *Дарвинизм: Критическое исследование*. Том 2 (Издание М.Е. Комарова, С.-Петербург, 1889)].
34. Ugolev, A.M. *Evolution of Digestion and the Principles of Evolution of Functions: Elements of Modern Functionalism* (Nauka, Leningrad, 1985) [Publ. in Russian: Уголев А.М. *Эволюция пищеварения и принципы эволюции функций: Элементы современного функционализма* (Наука, Ленинград, 1985)].
35. Ugolev, A.M. *Natural Technologies of Biological Systems* (Nauka, Leningrad, 1987) [Publ. in Russian: Уголев А.М. *Естественные технологии биологических систем* (Наука, Ленинград, 1987)].
36. Altshuller, G.S. *The Innovation Algorithm* (Technical Innovation Center, Worcester, MA, 2007). Translated from the Russian Second Edition, 1973, original author's title: "The Algorithm of an Invention" [Алгоритм изобретения].
37. Eigen, M. Self-organization of matter and the evolution of biological macromolecules. *Naturwissenschaften* **58**, 465-523 (1971).
38. Segré, D. & Lancet, D. Composing life. *EMBO Reports* **1**(3), 217-222 (2000).
39. Harms, J.W. Die Realisation von Genen und die consecutive Adaption. 1. Phasen in der Differenzierung der Anlagenkomplexe und die Frage der Landtierwerdung. *Ztschr. Wiss. Zool.* **133**, 211-397 (1929).
40. Harms, J.W. *Wandlungen des Artgefüges. Unter natürlichen und künstlichen Umweltbedingungen* (Johann Ambrosius Barth Verlag, Leipzig, 1934).

Acknowledgments

I would like to thank my brother Alexei L. Vyssotski, my wife Oxana O. Litvin, my daughter Vera Vyssotski, my father Leonid L. Vyssotski and my mother Natali V. Vyssotski (Segal).

Additional information

Supplementary Information accompanies this paper at http://www.evolocus.com/evolocus/v1/evolocus-01-025-s.pdf

Competing financial interests: The author declares no competing financial interests.

How to cite this article: Vyssotski, D.L. Nomogenesis and the logic of chance. *Evolocus* **1**, 25-30 (2016). www.evolocus.com/evolocus/v1/evolocus-01-025.pdf

Received 28 June 2016; **Accepted** 30 June 2016; **Published** online 17 July 2016