

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/312452601>

# A resonance based model of biological evolution

Article in *Physica A: Statistical Mechanics and its Applications* · April 2017

DOI: 10.1016/j.physa.2016.12.016

CITATIONS

0

READS

3,091

2 authors:



[Achille Damasco](#)

University of Naples Federico II

1 PUBLICATION 0 CITATIONS

[SEE PROFILE](#)



[Alessandro Giuliani](#)

Istituto Superiore di Sanità

462 PUBLICATIONS 5,567 CITATIONS

[SEE PROFILE](#)

Some of the authors of this publication are also working on these related projects:



Recurrence quantification analysis on otoacoustic emissions [View project](#)



Percolation properties of amino acid networks [View project](#)

All content following this page was uploaded by [Alessandro Giuliani](#) on 26 January 2017.

The user has requested enhancement of the downloaded file.



# A resonance based model of biological evolution



Achille Damasco<sup>a,\*</sup>, Alessandro Giuliani<sup>b</sup>

<sup>a</sup> *Università di Napoli Federico II, Department of Physics, Strada Vicinale Cupa Cintia, 21, 80126, Napoli, Italy*

<sup>b</sup> *Istituto Superiore di Sanità, Environment and Health Department, Viale Regina Elena 299, 00161, Roma, Italy*

## HIGHLIGHTS

- A model relies on forced harmonic oscillator for evolution is proposed.
- Macroevolution is described as a resonance phenomenon.
- It presents a hypothesis for the so-called Cambrian Explosion.
- The model provides also an explanation for periods of evolutionary stasis.

## ARTICLE INFO

### Article history:

Received 7 January 2016

Received in revised form 1 September 2016

Available online 21 December 2016

### Keywords:

Phase transitions

Physical models

Cambrian explosion

Theory

## ABSTRACT

We propose a coarse grained physical model of evolution. The proposed model ‘at least in principle’ is amenable of an experimental verification even if this looks as a conundrum: evolution is a unique historical process and the tape cannot be reversed and played again. Nevertheless, we can imagine a phenomenological scenario tailored upon state transitions in physical chemistry in which different agents of evolution play the role of the elements of a state transition like thermal noise or resonance effects. The abstract model we propose can be of help for sketching hypotheses and getting rid of some well-known features of natural history like the so-called Cambrian explosion. The possibility of an experimental proof of the model is discussed as well.

© 2016 Elsevier B.V. All rights reserved.

## 1. Introduction

According to established theory, random genetic mutations and natural selection are the phenomena that act as the core engine for the evolution of the species [1].

Random mutations are modifications along the sequence of the DNA, mainly due to replication errors, so that ‘random’ means that they are the product of individual causes that we ignore and cannot have control on it and, still more important, are unrelated with the organism fitness.

In addition to these two (classical) factors, epigenetic phenomena are rapidly gaining momentum [2,3]. We can roughly define epigenetic changes as variations of the phenotype of an organism due to a modification of the gene expression pattern without modifications of the DNA’s sequences.

Random mutations, natural selection and epigenetic changes have been taken under consideration to generate a theoretical frame to the ‘saltation-and-stasis’ phenomenology suggested by fossil records [4,5].

Fossil records show a highly non-linear trend of the evolution, made of long period of standstill interrupted by relatively fast appearances of many species. The Gould and Eldredge ‘Punctuated Equilibria’ theory interprets the alternation between

\* Corresponding author.

E-mail address: [achille.91@live.it](mailto:achille.91@live.it) (A. Damasco).

<http://dx.doi.org/10.1016/j.physa.2016.12.016>

0378-4371/© 2016 Elsevier B.V. All rights reserved.

'saltation' and 'stasis' keeping the idea that evolution is characterized by the combined effect of random mutations and natural selection, although in some situations its speed may be very low [5].

Nowadays, the discovery of the lack of bi-univocal character of the genotype–phenotype relation [6,7] and the overwhelming combinatorial complexity of molecular interaction (Tompa and Rose in their paper [8] gave a gross estimate of  $10^{7200}$  molecular interaction constraints to be satisfied in a relatively simple system like yeast) push to try to face evolution non-linearity with a fresh perspective.

Here we try to sketch a plausible frame of evolution building upon the three basic evolution pillars: stochastic nature of DNA mutations, epigenetic changes and selective pressure. Our goal is to insert these three pillars in the frame of the physical theory of forced harmonic oscillators. We do not propose a 'definitive mathematical theory of evolution' but we hope this exercise can be useful for hypothesis generating.

We build upon the universal character of state transitions displaying some largely invariant features across different fields of application such as cell differentiation, finance and physical chemistry (see for example Refs. [9–12]). The exercise to fit evolution into the general frame of state transitions allowed us to accommodate both stochastic and directional effects and to generate some implications on evolutionary biology.

## 2. Evolutionary model

The main actor of the proposed model is a biological species defined as a vector in a  $N$ -dimensional space, where  $N$  is the number of characters that describes that species. We associate to each of the  $N$  characters an axis representing all the possible expressions (not only those actually observed) of that character. We call  $X$  the coordinate of a species on one of these axes. A given  $X$  will correspond to the value taken for one (out of the  $N$  defining the space) character by a species that, in turn, is a point associated to a unique configuration in the  $N$ -dimensional space. Thus, the value of  $X$  corresponds to a certain phenotype. Each species encompasses many individuals, so we intend the  $X$  of a given species as the 'average' phenotype.

It is worth focusing on the abstract nature of our model so, at this point, we give for granted the mutual independence of the variables spanning the space.

The phenotypic  $N$ -dimensional space must be intended as the co-domain of a domain  $Z$  represented by the genotype. The vector points in this space thus correspond to the single individuals that belong to the species.

Since every living organism by definition eats, grows and reproduces, the configuration of a particular character that best ensures a species in its habitat to perform these functions will be a point  $X$  which we will call  $X_0$ , i.e.  $X_0$  is the point of maximum fitness.

If we add another dimension which indicates the allelic frequency  $f$  of a certain character set, namely the number of times it appears in a population divided by the number of individuals of that population, then we can build an allelic frequency distribution. Such allelic frequency will follow a Gaussian; that is, if we consider the  $N$ -dimensional space of the characters as the domain of  $f$  (which is a function in  $N$  variables, i.e.  $f = f(X_1, X_2, \dots, X_N)$ ) we expect the top of the distribution (the maximum of  $f$ ) corresponds to a particular point of the  $N$ -dimensional space. In the case of considering only one character, that point is  $X_0$ . This corresponds to say that the 'optimal configuration' tends to be the most frequent.

In the following, we will introduce the hypotheses at the base of the proposed theoretical model.

### 2.1. First hypothesis: harmonic oscillator

Now let us assume, for one character, that the typical effect of random mutations and natural selection is an oscillation of the actual point  $X$  around the peak of allele frequency, so that point generally will not be in  $X_0$  but at a coordinate we will call  $X_{MAX}$ .  $X_{MAX}$  in turn will swing around  $X_0$  with a harmonic motion given by

$$X(t) = A_0 \cos(\omega_b t) \quad (1)$$

In (1),  $X(t)$  is the coordinate of  $X_{MAX}$  at time  $t$ ,  $A_0$  is the amplitude of the oscillation and  $\omega_b$  is the frequency of the oscillation (i.e. the frequency by a constant factor equal to  $2\pi$ , for which hereinafter we will call the frequency  $\omega$ ). Such  $\omega_b$  is given by

$$\omega_b = \frac{2\pi}{T_0} \quad (2)$$

with  $T_0$  oscillation period of  $X_{MAX}$ . In turn

$$T_0 = \frac{m}{\lambda}$$

where  $m$  is a positive integer that represents the number of mutations that result in an oscillation of  $X_{MAX}$  while  $\lambda$  is the rate of mutations, which is by definition given by

$$\lambda = \frac{1}{n\tau}$$

where  $n$  is a positive integer that indicates how many generations are needed on average to observe a hereditary mutation and  $\tau$  is the average time interval for a given species between a generation and another (in the case of asexual organisms, between a cell division and another). Combining all the above equations we get the expression for  $\omega_b$ :

$$\omega_b = \frac{2\pi}{mn\tau} \quad (3)$$

The parameters  $n$ ,  $m$ ,  $\tau$  could, at least hypothetically, be experimentally derived.

The motion of  $X_{MAX}$  can be equated to that of a mass subjected to a return force, where such a force corresponds to the natural selection (remember we made the hypothesis of a species centered near a fitness maximum). Random mutations cause the displacement from  $X_0$ : a big removal from the configuration of maximum fitness will correspond to a great effect of natural selection and vice versa.

### 2.2. Second hypothesis: environmental factors

We add another hypothesis to our model. We consider an ecosystem as a structure describable by a set of quantifiable parameters, something like the average temperature of a given habitat, the moisture, the concentration of a given gas in the air or in the water, the density of individuals of species different from that taken into account, and so on.

Let  $P$  be one of the above parameters. We postulate that, if an ecosystem is in a situation of equilibrium,  $P$  has a given average value (in time). If the environment shifts to a new equilibrium state characterized by a different value of  $P$ , then, during the transient phase, the value of  $P$  will oscillate between the initial and the final value with a frequency  $\omega_E$ . The subscript “E” stands for “external” because  $P$  describes the ecosystem of our population, not the population itself.

We assume further that such  $\omega_E$  (which value can in principle be experimentally estimated) will be higher, the smaller the time interval needed for the environment state transition.

### 2.3. Third hypothesis: resonance

To model the discontinuous trends of evolution, we need to add a third and final key assumption in our model. We select from the whole set of parameters describing an ecosystem  $P$ , a subset of parameters (the existence of which depends on the species in question and must be sought experimentally) able to exert heritable epigenetic effects on a part of our population (see Refs. [13,14]). In other words, we assume that there exists the possibility that an “external” factor contributes to cause the displacements of  $X_{MAX}$ , but in this case, the time course of such displacements will be given from that of the external parameters (that is, it will not be necessarily harmonic).

We can now state the third hypothesis: if one of the parameters capable of epigenetic changes is swinging with frequency  $\omega_E$  because it is in a transient phase, then our species will evolve (so far at least as regards the considered character) if the following equality occurs

$$\omega_b = \omega_E \quad (4)$$

This relation, called Condition of Evolution (CE), is derived from the properties of a forced harmonic oscillator. Recovering our physical analogy, during a transient epigenetic effect, the external force characterized by the harmonic frequency  $\omega_E$  causes a resulting motion of  $X_{MAX}$  described by the law

$$X(t) = \frac{a_E \cos(\omega_E t)}{\omega_b^2 - \omega_E^2} = A_R \cos(\omega_E t) \quad (5)$$

where we define

$$A_R = \frac{a_E}{\omega_b^2 - \omega_E^2}$$

in which  $a_E$  is a constant equal to the amplitude of the oscillation that would occur if the “external force” were constant over time. Note that the argument of the cosine is  $\omega_E$  because that is the property of forced harmonic oscillators for which  $\omega_b$  tends to  $\omega_E$  if at first  $\omega_b \neq \omega_E$  (with consequences which we will discuss later).

From these two relations we see that in the limit of  $\omega_E$  going to  $\omega_b$ ,  $A_R$  diverges, i.e. the point  $X_{MAX}$  explores regions (at least in theory) indefinitely away from its original basin of attraction. During this motion the system traverses a rugged fitness landscape, visiting potentially new points of maximum fitness. This behavior can be considered as a resonance which, in our case, describes the transition from one species to another. In other words, this can be interpreted as a mechanism for macro-evolutionary changes.

We can describe also the case of evolution with bifurcation into two species, because in that case the only difference is that we have more of a new point of equilibrium representing the new evolutionary forms; i.e. it goes through the evolution from point  $X_0$  to  $X_{0,A}$  and  $X_{0,B}$ .

In the realistic case in which the CE is not fulfilled perfectly but only in good approximation,  $A_R$  is a “space” the half of which will be covered in a time that we will call TE (Time Evolution). We can make an estimate of TE

$$TE \leq \frac{\pi}{\omega_b} = \frac{mn\tau}{2}$$

2.4. Corollaries

Exploiting other properties of a forced harmonic oscillator, we can add three corollaries to our evolutionary model.

1. If  $\omega_E \gg \omega_0$  then  $A_R$  tends to zero. The biological consequence of this corollary is that in the case of abrupt changes in the ecosystem, much greater than the adaptability of the population, the species could be extinguished because it loses the ability to oscillate in the neighborhood of the configuration of maximum fitness.
2. If  $\omega_0 \gg \omega_E$  then  $A_R$  tends to  $a_E/\omega_E$ . In this case the biological counterpart is a situation in which the external changes are slow compared to those of the population but there is no evolution (or even extinction), simply the amplitude of oscillation of the characters only changes of a constant factor.
3. If  $\omega_0 \approx \omega_E$  but it is neither the case of the resonance nor of the two previous limiting cases, it happens that  $\omega_0$  tends to coincide with  $\omega_E$ . Biological phenomena consistent with this corollary are all the numerous cases in which a living species adapts to an external oscillating parameter immediately assuming the same rate of change. Circadian rhythms are the by far most widespread examples of this situation (see Refs. [15,16]).

The next two corollaries describe more complex situations with respect to the very rough and simplistic concepts set forth in the constitutive assumptions of our model.

4. If the changes of the ecosystem are not harmonic but only periodic with period  $T$ , then we use as  $\omega_E$  the main harmonic and eventually the first subsequent of the development in Fourier series of changes in the ecosystem:

$$f(t) = a_0 + \sum_{M=1}^{\infty} a_M \cos \frac{M\pi t}{T} + b_M \sin \frac{M\pi t}{T}$$

where  $f(t)$  is the function that expresses the changes over time of the parameters  $P$ .

In the case it should be possible to apply an analytic function (at least in first approximation),  $a_0$ ,  $a_M$  and  $b_M$  coefficients estimate the relative weights of terms of the development and, for every  $M$ ,  $(M\pi/T)$  are the harmonic of the development.

Although the summation goes from 1 to infinity, only a finite number of terms will be biologically influential because subsequent terms weigh less and less than previous ones, and higher order ones correspond to variations to which a species is practically insensitive to. We note that for orders below that limit, what interests us are the frequencies of the development and not the coefficients because the resonance phenomenon depends only on them and not on the amplitudes. This is an advantage in the case it is impossible to model the changes in the ecosystem by an analytic function and consequently we have not the possibility to compute the coefficients of the expansion.

If we apply the fourth corollary to the CE we obtain an equivalent form, in fact by

$$\omega_0 = \omega_E$$

replacing the expressions of the frequencies we obtain

$$\frac{2\pi}{m\pi} = \frac{M\pi}{T}$$

explaining  $M$  we obtain

$$M = \frac{2T}{m\pi}$$

but remembering that  $1/(n\pi) = \lambda$  we can write the final relation in a more compact form

$$M = \frac{2\lambda T}{m}$$

this last relation is equivalent to the CE but it regards cases of external variations that are periodic but not strictly harmonic and postulates that evolution takes place if the product of the constants that appear at the second member is equal to a small integer.

The last corollary we propose does not present a full relation but only an indicative one of the mathematical form that will have a significant element of our model, the probability of evolution:

5. If the ideal case  $\omega_0 = \omega_E$  is not realized, the evolution will occur with a probability given approximately by

$$P = \prod_{i=1}^N \prod_{n=1}^M A(\omega_{n,i})/A_{TOT,i}$$

where  $N$  is the number of characters epigenetically modified by the parameters of the ecosystem,  $M$  is the number of harmonics which can approximate the trend of the ecosystem within the sensitivity of the species,  $A_{TOT,i}$  is the amplitude of the entire space of variation of the  $i$ th character,

$$A(\omega_{n,i}) = \frac{a_E}{\omega_i^2 - \omega_{n,i}^2}$$

where  $a_E$  is again the amplitude if the “external force” is constant,  $\omega_i$  is the frequency with which oscillates the  $X_{MAX}$  of the  $i$ th character and  $\omega_{N,i}$  is the  $n$ th harmonic that is approximately equal to  $\omega_i$ .

We need to give further details about the quantity  $N$ : among characters modifiable by means of external factors should not be counted those that appear only thanks to such factors (thus those which would increase a degree of freedom of the space characters) and even those that disappear. In the first case the  $\omega_i$  for that character cannot be defined, so it cannot produce resonance; in the second case the impossibility of the CE is trivial.

Of course, if one or more addends in the double summation are greater than 1, then we must consider  $P = 1$ , in particular if  $\omega_i = \omega_{N,i}$  for at least one index  $i$  we come back to the case of perfect resonance.

In summary, if there is not perfect equality in the CE, the probability of evolution is greater the more

- (1)  $\omega_{N,i} \rightarrow \omega_i$  (i.e. how much closer it is to resonance)
- (2)  $N$  is greater (i.e. the more the species is complex and sensitive to the environment)
- (3)  $M$  is greater (i.e. if the alteration of the ecosystem is periodic but not harmonic, evolution is facilitated).

So far, we have considered the characteristics of a population as independent of each other, but this hypothesis is far from realistic. In general, given a character  $x(t)$  which oscillates with harmonic motion around its most frequent value, it will exist at least another character  $y(t)$  such that  $y = y(t, x(t))$ . This second character also will have its peculiar oscillation in time but also a certain dependence from changes of  $x(t)$ .

For the purposes of the realization of the CE, the ways in which characters mutually interact can be divided into two classes: those that involve a resonance for both when it is realized for one of the two and those in which this resonance does not happen.

Mathematically the first case is expressed by saying that

$$\lim_{x \rightarrow y} y = \pm \rightarrow. \quad (6)$$

For example, the (6) is certainly satisfied in the case of  $y(t) = A'_0 x(t) \cos(\omega'_0 t)$ , that is, the character  $y$  oscillates with its own frequency  $\omega'_0$  but its amplitude is proportional to  $x(t)$ .

All this implies a modification of the formula which provides the indicative estimate of the probability of changing, so it becomes

$$P = \prod_{i=1}^M \prod_{n=1}^N \gamma_i A(\omega_{n,i}) / A_{TOT,i}$$

where

$$\gamma_i = \begin{cases} \frac{A_{l,i}}{A_{TOT,l,i}} & \text{if } Q \neq 0 \\ 1 & \text{if } Q = 0 \end{cases}$$

where  $Q$  is the number of characters that depend from the  $i$ th character and that have a dependency on this that satisfies (6) (they are indexed by  $l$ ),  $A_{l,i}$  is the amplitude of oscillation of the character  $l$ th and  $A_{TOT,l,i}$  is the amplitude of the entire space of variation of the  $l$ th character.

If we consider that any positive magnitude (in our case the amplitudes of oscillation) when multiplied by a number between 0 and 1 (in our case  $\gamma_i$  when  $Q \neq 0$ ) becomes smaller (that is, tends to zero), then our model implies that a species with characters that are all oscillating, and for the most part linked between them, has a virtually null probability of evolution in response to external factors that are not next to the CE and, at least in theory, a probability of evolution that rapidly tends to 1 for  $\omega_E \rightarrow \omega_b$ .

This just described situation is compatible with all those cases in which a species is adapted to a variation of one or more external factors resorting to variations already available in its gene pool without therefore having to evolve into “other”. At the same time it includes the probable feature of evolution to manifest only in the presence of external factors strongly calibrated on the CE.

In summary, adding contributions of all the characters modified by a given epigenetic factor and interactions between the characters, the mechanism based on the resonance becomes, for the entire species, similar to a phase transition (i.e., it has a non-linear and threshold behavior). Moreover, our model can be generalized if instead of an epigenetic factor is considered another type of variation, which however plays the same role of ‘oscillating driver’ endowed with heritability even for only few generations.

### 3. Special evolutionary phenomena in the light of the proposed model

We can look at some episodes in the history of life on Earth so to reinterpret them in the language of our evolutionary model. This is, in our opinion, a useful exercise to check the plausibility of the proposed frame.

### 3.1. Stasis of the pre-Cambrian

We start from the long evolutionary stasis that fossils recorded in the time range from about 2 billion years ago (the appearance of eukaryotic organisms) to about 500 million years ago (early Cambrian). In this time interval the evolution, if we quantify it by the number of species appeared from an initial moment up to an arbitrary time, looks as being in a stand-by mode for one and a half billion years, which represents a major portion of the entire evolutionary history.

This stagnation can be explained in the light of the formula (3) and in the second corollary: since the unicellular organisms have a very short life cycle ( $\tau$  very small), then their  $\omega_b$  will be very high. This is the situation described by the second corollary, that is, we do not have either evolution or extinction. With a  $\omega_b$  extremely high, it is highly improbable that environmental changes could take place so to ensure the resonance, whereby the stasis has characterized this long time interval.

### 3.2. Cambrian explosion

The opposite phenomenon happened at the beginning of the Cambrian and has been defined as “Cambrian Explosion”. It consisted in the appearance in relatively short geologic time of most phyla of complex animals and the diversity of living species began to be similar to the current [17].

In the frame of our proposal, we can explain the explosion as the combination of two factors: the first was the relatively rapid succession of relevant climatic and geologic changes pushing toward the realization of the CE. The second factor was a situation in which existing species before explosion were very similar to each other (i.e. they all had similar  $\omega_b$ ) so to make it possible a “mass evolution” that, by observing the expression of  $T_E$  (time evolution) was in this case also very rapid.

### 3.3. Quantitative uniqueness of the Cambrian explosion

To complete the discussion on the Cambrian explosion we note that other “explosions” took place in subsequent times, but these were not of the same scope as the Cambrian. This peculiarity could be explained by the fact that following the differentiation of the organisms, each species had a different  $\omega_b$  for which, for the same environmental changes, there no longer existed the factor of reciprocal similarity of the oscillation frequency of the characters.

### 3.4. The Mesozoic

An interesting further application of our model is the analysis of the Mesozoic period, from about 251.0 to about 65.5 million years ago that it is known as the “Age of Dinosaurs”. The Mesozoic was characterized by the dominance of reptiles, especially many species of dinosaurs, while mammal species similar to the current mice and the first small birds made their first appearance. As we know, this situation is reversed with the famous extinction of the dinosaurs (and many other species of the time). Let us see how to describe these events with the Model of Resonances.

During this period the climate was very stable, so, in our language, there was a small  $\omega_E$  that easily resonates with the low  $\omega_b$  of the dinosaurs and of all other long-lived animals (greater than that of the first mice and early birds). Following a catastrophic event (i.e. the hypothesized fall of a big meteorite) and for dramatic climate changes there was  $\omega_E / \omega_b$  of the dinosaurs (and then, for the first corollary, there was the extinction), while  $\omega_E \approx \omega_b$  of the other animals (which evolved).

Note finally that during the early Mesozoic mammals and birds not dominated but were still present because they fulfil the second corollary ( $\omega_E \ll \omega_b$ , i.e. no extinction or evolution).

## 4. Conclusions

We cannot deny that in order to realize an experimental verification of the proposed physical frame, we must face the completion of the theoretical model and the practical realization of an experiment that tests it.

The first problem is, given a certain living species, the identification of the subset of ecosystem parameters  $P$  that have a heritable epigenetic effect on the species under consideration. Such identification is not easy because while epigenetics microscopic features are starting to be elucidated, the heritability of epigenetics changes is a still largely obscure area.

The second problem concerns the difficulties of estimating the actual values of mutation rates and of  $m$  (only known for specific laboratory conditions), and the realization of a device and/or a procedure in allowing us to vary the above-mentioned parameters  $P$  so to force them into a periodic behavior which satisfies the CE. This oscillatory behavior should not only be controlled but also finely tuned. It is well known that living organisms have a great adaptation ability to “external forcing” making it very difficult to impose an external ‘periodic force’ forcing a population to evolve.

In the language of our model, it is like saying that it is very easy to fall in the third corollary but is difficult to achieve resonance.

In summary, an experimental verification can only be operated on a very simple system under highly artificial circumstances.

Stimulated by explanatory aspects that our model seems to show, we hope that we can move forward in its development solving the two problems just stated. In any case we are convinced that, even on a purely metaphorical level, the definition of a general physically motivated model of evolution could be of inspiration for evolutionary biologists for choosing potentially interesting observables.

## References

- [1] P.H. Harvey, M.D. Pagel, *The Comparative Method in Evolutionary Biology*, Oxford University Press, Oxford, 1991, p. 239.
- [2] D. Noble, E. Jablonka, M.J. Joyner, G.B. Mueller, S.W. Omholt, Evolution evolves: physiology returns to centre stage, *J. Physiol.* 592 (2014) 2237–2244.
- [3] M. Slatkin, Epigenetic inheritance and the missing heritability problem, *Genetics* 182 (2009) 845–850.
- [4] S. Urdy, L.A. Wilson, J.T. Haug, M.R. Sánchez-Villagra, On the unique perspective of paleontology in the study of developmental evolution and biases, *Biol. Theory* 8 (2013) 293–311.
- [5] Stephen Jay Gould, Niles Eldredge, Punctuated equilibria: the tempo and mode of evolution reconsidered, *Paleobiology* 3 (1977) 115–151.
- [6] E. Reuveni, A. Giuliani, Emergent properties of gene evolution: Species as attractors in phenotypic space, *Physica A* 391 (2012) 1172–1178.
- [7] A. Crombach, P. Hogeweg, Evolution of evolvability in gene regulatory networks, *PLoS Comput. Biol.* 4 (2008) e1000112.
- [8] P. Tompa, G.D. Rose, The Levinthal paradox of the interactome, *Protein Sci.* 20 (2011) 2074–2079.
- [9] M. Scheffer, S.R. Carpenter, T.M. Lenton, J. Bascompte, W. Brock, V. Dakos, van de Koppel, I.A. van de Leemput, S.A. Levin, E.H. van Nes, M. Pascual, J. Vandermeer, Anticipating critical transitions, *Science* 338 (2012) 344–348.
- [10] A.N. Gorban, E.V. Smirnova, T.A. Tyukina, Correlations, risk and crisis: From physiology to finance, *Physica A* 389 (2010) 3193–3217.
- [11] M. Tsuchiya, A. Giuliani, M. Hashimoto, J. Erenpreisa, K. Yoshikawa, Emergent self-organized criticality in gene expression dynamics: Temporal development of global phase transition revealed in a cancer cell line, *PLoS One* 10 (2015) e0128565.
- [12] P.B. Gupta, C.M. Fillmore, G. Jiang, S.D. Shapira, K. Tao, C. Kuperwasser, E.S. Lander, Stochastic state transitions give rise to phenotypic equilibrium in populations of cancer cells, *Cell* 146 (2011) 633–644.
- [13] C.A. Cooney, A.A. Dave, G.L. Wolff, Maternal methyl supplements in mice affect epigenetic variation and DNA methylation of offspring, *J. Nutr.* 132 (8 Suppl.) (2002) 2393S–2400S.
- [14] R.A. Waterland, R.L. Jirtle, Transposable elements: Targets for early nutritional effects on epigenetic gene regulation, *Mol. Cell. Biol.* 23 (15) (2003) 5293–5300.
- [15] Z. Gerhart-Hines, M.A. Lazar, Circadian metabolism in the light of evolution, *Endocr. Rev.* 36 (2015) 289–304. <http://dx.doi.org/10.1210/er.2015-1007>.
- [16] K.J. Schippers, S.A. Nichols, Deep, dark secrets of melatonin in animal evolution, *Cell* 159 (2014) 9–10.
- [17] R.K. Bambach, A.M. Bush, D.H. Erwin, Autecology and the filling of Ecospace: Key metazoan radiations, *Palaeontology* 50 (1) (2007) 1–22.