Hungarian Studies Yearbook
2019 (I)

sciendo DOI: 10.2478/HSY-2019-0010

Embracing Noise and Error

Bálint L. BÁLINT
University of Debrecen, Department of Biochemistry and Molecular Biology; e-mail: lbalint@med.unideb.hu

ABSTRACT:
In his article "Embracing Noise and Error", Bálint L. Bálint argues that human society is going through a profound change as mathematical models are used to predict human behavior both on a personal level and on the level of the entire society. An inherent component of mathematical models is the concept of error or noise, which describes the level of unpredictability of a system by the specific mathematical model. The author reveals the educational origin of the abstract world that can be described by pure mathematics and can be considered an ideal world without errors. While the human perception of the world is different from the abstractions we were taught, the mathematical models need to integrate the error factor to deal with the unpredictability of reality. While scientific thinking developed the statistic-probabilistic model to define the limits of predictability, here we present that in a flow of time driven by entropy, stochastic variability is an in-built characteristic of the material world and represents ultimately the singularity of each individual moment in time and the chance for our freedom of choice.

Keywords: models, error space, freedom, variability, overfitting, noise, prediction.

We are living in a world of data. Sentences like "data is the new oil" are raising the importance of a better understanding of the relationship between us, or in general the individual person at a given time, and the immense amount of data collected about our life by others. Ownership of data and implications of predictions performed with these data is raising reasonable concerns. While data itself is a pure descriptor, the models built on these data can be of great value and allow interventions that are able to shape the future. While personal data could be assigned as a property of the individual, the ownership of the developed mathematical models based on these data is definitely a more complex question. The acquisition, storage and development of these models is beyond the capacities of the average person and therefore the ownership issue is more complex. The presence of mathematical models in our everyday life became emerging with the availability to collect data and at the same time to process and build models in a fast and cheap manner. Instruments, sensors, data storage and data format standards provide the foundation for large scale data acquisition. Models describe our life, from our shopping habits to our online activity, from weather monitoring to stock exchange predictions: everything is monitored and processed. The collected data is processed and mathematical models are built that aim to a better prediction of what will happen in the future. These mathematical models have tremendous and immediate value, for example in stock exchange brokering, but also obvious limitations as we all see in the accuracy of the weather forecast. Economic models, shopping prediction, political manipulation with targeted messages of subgroups of individuals are all present in our everyday life and try to rule our everyday decisions. Indeed, these models are tiny and opaque windows to the future and knowing the future allows us to modify our current decisions to have a benefit of future developments.

While we could consider this big data era as a source of danger and manipulation, we have to see also that building a mathematical model is just a novel, automated method of learning. Concepts as "deep learning" or "neural networks" pinpoint that automated, computer-based learning and human learning itself are methods that have very much in common and both of these can be considered methods of modelling. Indeed, learning is a way to make accurate predictions in a space that is widening as a person is leaving home, then graduating and later becomes an active, contributing member of the society. Learning is a continuous process of building models that help us to solve problems we have not faced before. Simulations and extrapolating earlier personal or collective experience can help us to understand the consequences of a specific situation. As a result, we can develop ways to behave in never before experienced situations in order to solve these ones and ultimately to influence them. The novelty of the last decade, besides the never before seen amount of collected data, is that learning became an automated procedure, where computers build models to predict the future and the human component of learning is decreasing.

When we speak about mathematical models, we need to acknowledge that one constant component of these models is the concept of error. Error is the difference between an individual data point and the mathematical model that describes the overall system. The model building methods are trying to decrease the overall error of a model. These errors create an "error space" (Cen and Luo, "Error-Space"; Fisher et al., "Distributions"). The error space is a space where anything is feasible, and the model cannot predict the behavior of any data points within this space. This error space is the space of unpredictability, it is the space of individual variability and as such is the space of freedom, stochastic variability, freedom from the models and therefore it is coined in statistics as "degrees of freedom"(Pandey and Bright, "What Are Degrees of Freedom?") (Janson, Fithian, and Hastie, "Miscellanea").

Interestingly there is an optimal level of accepted error of a model and decreasing below this level is considered "overfitting" – although the data points used for building the model are better described, the prediction value of the model is decreasing, which means that novel data points collected in the same setting will not follow the model that is overfitted to the data points. Overfitting is tested by subsetting the available data points and testing the performance of the model with different levels of variability, namely different accepted error rates (James et al., *An Introduction to Statistical Learning*). Ideally, the best model is that which is not depending on the particular subset of a large dataset and therefore newly acquired data points will be described accurately with a defined error factor by the model. The observed problem of overfitting means also that the error space cannot be reduced below a limit and it is an inherent component of any observed phenomenon. This observation draws our attention to a certain level of unpredictability of real-life events and ultimately to the freedom within certain limits of any real-life observation. Any attempt to overfit, namely to predict what is unpredictable, to constrain reality within narrow limits of rules will fail as this is proven by the experience of overfitting. Overfitting coins also that there is no absolute or ideal set of rules that describe real-life events and remind us humbly of the Gödel rules that state that even in an abstract mathematical world there will be some aspect that cannot be answered within that space (Gödel, "Über Formal Unentscheidbare Sätze").

The concept of error in some cases is coined as noise. The concept of noise mirrors the concept of signal and defines that the perception of the signal is altered, distorted by other external or internal factors and the ability to perceive the signal is decreasing as the noise is increasing. While noise, similar to the notion of error, has a clear negative connotation and seems to be a random component, we can understand better the space of individual variability if we consider the interpretation by several musicians of the same piece of classical music. While all of them will be different, the concept of noise is probably not the cause of these individual differences. The individual differences are imprints of the skills, personality and framework of interpretation of the notes provided for each artist. Modelling, in this case, would be the creation of a new music sheet based on simple listening to the music played by several musicians. Overfitting would be the inclusion of the personal variances present in the interpretation of all individual musicians. What we refer to in our investigation here is this space of variability that is not really a space of error and not even a space of noise but it is a space of individual variability. Similar distinctions between the perfect and the actual manifestation are known in arts, music, theater and we leave these to the reader to contemplate about the relationship between individual and ideal and consider if the error is indeed the best word to name these differences.

If we try to understand why the term error is used to describe the difference in a mathematical model from the real-life event, we will probably need to go back to our schooling system where we were taught that a point has no dimensions, a line has no width and a plane has no thickness. We had to believe our teachers and a substantial effort in abstraction needs to be performed by every child to accept these statements, as all his previous observations in the real world dramatically contradict these abstractions. On the other hand, these abstractions allow us to simplify problems and help us to make easy calculations on everyday use cases from how much seed is needed per acre of land or how much paint is needed to paint the wall of a room. These abstractions help us to make calculations and we usually accept to calculate with margins of errors for these everyday tasks. The world of mathematics is an absolute world without errors, where a point has no dimensions and parallels never meet, it is a simple world where predictions are done relatively easily. This absolute, ideal world is originated in the platonic worldview where pure ideas rule the world. We can state that these abstractions helped tremendously the development of science to the current level. Moreover, these concepts of pure perfection and an ideal world are present not only in science but probably in all aspects of life from arts to religion. On the other hand, in the last two centuries, error and noise, imperfectness and transient components or the individual characteristics of a piece of art or a mathematical model became an important and valid component both in art and science and exploring this space is absolutely accepted as valid. The interface between perfection immanent in modern art and the understanding of error, noise or stochastic components of larger systems in science are bringing us closer to understanding our own life in a deterministic space and to address fundamental questions such as the question of freedom of choice or time in the context of life and death.

The mathematical tool that contributed to a large extent for a better understanding of the difference between pure science and real-world events, was the development of statistics. Interestingly, in statistics we address the concept of variability by building a novel set of abstractions that are not present in the everyday reality, for example, a perfect normal distribution is never achieved but we still use the normal distribution as a basis of statistical calculations. Statistics relies on the concept that repeated measurements are in most cases different from each other. If we measure the length of a piece of marble, the difference comes from the different tools used for measurement or the different persons who are measuring it. In this case, we assume that there is an absolute length of the marble and the differences in measurements are simply errors. If we measure a living organism plant or animal, the factor of time has a much larger influence on the measurement than in the case of a marble. Depending on the used tools we can have very good approximations on the actual height of a person but the more precise the measurements are the higher chance is that measurements will differ from each other. If we measure the height of the students in a class, we will see that these values will be very different. The statistical approach to express the height of the students of a class is giving the average and standard deviation, namely the average distance of individual heights from the average. The abstraction of the height of the students in a class is provided by a statistical description of the members of the class. This is an important distinction as other approaches would also be possible. We could consider one person that is not too high and not too low (the median value) in the class, or we could make bins and identify which is the most abundant bin (the modus) and consider these values as "representative" values. Selecting representative values would consider those values as ideal/typical values and all the other ones as differing due to "errors". The statistical approach is never refraining to a particular case but to the population itself in its multitude. The error space is the space where individual and particular events are present as a multitude.

If we leave the ideal world, for a better understanding of the individual variabilities coined as "error", and for a better understanding of the space where these particular events are distributed as individual entities, namely the "error space", we need to consider the concept of time. Time is an irreversible flow of the world determined by irreversible reactions (Gaspard and Wang, "Noise, Chaos")τ. Dispersion of energy in space is irreversible and dispersion of the ordered matter into the unordered matter is a general phenomenon of everyday life. Entropy is the increase of chaos, the decrease of order and movement that is driven by the inherent thermodynamic energy of every atom and molecule (Halliwell, Pérez-Mercader, and Zurek, *Physical Origins*). A clear and easy manifestation of time, entropy and irreversible movement is the dilution of a drop of ink in a glass of water. Brownian movement of water molecules will create a uniform solution and while the solution exists, it will stay mixed. Separation of ink and water is possible but not spontaneously in the context of the solution. A series of events (like evaporation, filtration etc.) can separate the water and the ink but this novel state will not be equal with the original state, it will be the third state in time and space, also irreversible and unique as the mixing of ink and water.

Entropy is defining an irreversible flow of events (Varotsos et al., "Some Properties of the Entropy"). To be noted that entropy is likely to be a pure abstraction, as on a cosmic level nothing indicates that we live in a world that is static, uniform and infinite. In an ideal mathematical world noting should be irreversible and the movement of atoms and molecules is not fully random but defined by specific laws, everything is predictable and reversible. As a consequence, we can also state that in the world of ideas, time is not existing in a similar way as our every-day perception of time exists. In the world of ideas, a point has no dimensions and any moment can be turned back to any prior position. As such, we can come to the same conclusion that has been stated several times, namely that time is linked inherently with matter and the energy dissipation or entropy in the material world is the basis of the irreversibility of time.

Ervin Schrödinger in his three lectures at Trinity College, Dublin (1943) and later in his essay published with the title "What is life?" (1992) argues that the inherent uncertainty seen on the subatomic level is equilibrated on a dimension that is larger by orders of magnitude than the level of atoms, and this is why the smallest stable biochemical systems are formed at the size of known cells. Smaller structures would behave unpredictably as a consequence of subatomic random variation, but on the level of cellular structures, this subatomic random variability is equilibrated and allows stable function. The contribution of Brownian movement and entropy to his concept can be described by the statistic deterministic model where laws describe the behavior of a system with a relatively good approximation. While the error is an accepted component of these systems, its contribution to long-term predictability of such systems was not addressed in depth in the essay. A very important concept of statistics and of our everyday life is the concept or error propagation. By error propagation, we mean that if two components that have their own error rate interact, the sum of the interaction will be an output in which the two errors are summed. The error propagation in complex systems makes long term predictions very difficult or even impossible. If we consider the weather forecast, we can make predictions about the actual weather in the range of days. We cannot predict exact weather on a longer scale than days due to the fact that any type of weather within a range characteristic to that specific location can be considered "normal". On the other hand, we can say with a good approximation that the chances to have snow in July in Jerusalem is very low and the chances not to have snow in the Alps in January is also very low due to the simple fact that these values are outside of the range of the degrees of freedom for that particular place. A similar phenomenon is true to the stock exchange variability, cell-to-cell variability and person-to-person variability on the level of societies too. For example, we all consider we have our freedom of choice and what we decide is a proud free decision of ourselves. If we go out for a walk, a coffee or shopping is the ultimate decision of ourselves. This is our ultimate freedom to make our own decisions. We can decide whether we go to sleep or stay up and work during the night. Yet on the level of a city with hundreds of thousands of inhabitants, we can clearly make statistics on how many people are at a coffee shop, how many are shopping or just walking. We can also count how many people are awake at 3 AM and based on these values we can describe the likelihood of staying up during the night for an average inhabitant of the city. While each person has his/her own freedom of choice, the activities of the city can be described relatively well with statistical approaches. We can even predict that the number of people sleeping during the night is by orders of magnitude larger than those who are sleeping at 11 AM. This model might have an error and anytime can happen that someone needs to stay awake exceptionally.

On a cellular level in the last decades, it became evident that cells behave like populations and even genetically identical cells can have relatively large variability in protein and gene expression without any clear explanation (Swanton and Beck, "Previews Epigenetic Noise"). It seems that even monoclonal, isogenic cells can express genes and proteins in a range of orders of magnitude (Ozgyin et al., "Extensive Epigenetic and Transcriptomic Variability")gene expression, and drug response. The extent of genotype-independent functional genomic variability of the LCL model, although largely overlooked, may inform association study design. In this study, we use flow cytometry, chromatin immunoprecipitation sequencing and mRNA sequencing to study surface marker patterns, quantify genome-wide chromatin changes (H3K27ac. These expression levels usually have a normal distribution on a logarithmic scale. This means that even genetically identical cells of the same differentiation state can have extremely different manifestations. Moreover, the whole population can shift if triggered by a particular signal although there is no evidence that the magnitude of change is identical for each and every cell, still, the whole population will be shifted to a new state.

Based on the examples above we can state that statistic deterministic models can describe both systems on a subatomic level, cellular systems, weather predictions, stock exchange predictions, even societies, and on all these levels models have error or variability rates that are inherent properties of real-life events. Moreover, the validity of these models is limited by the degrees of freedom of a particular component and the error propagation in complex systems. What seems obvious is that stochastic components of a large system equilibrate each other and result in a system that can be described with the statistic deterministic model. While these models can describe the system in general, their predictive value on the level of an individual component of the system is very limited. Individual components like a particularly unstable isotope, a cell, a person or the price of the next transaction with a particular share on the stock market are most likely unpredictable within certain limits, but these limits are wider than acceptable for everyday decisions.

The word error suggests that it is erroneous and there would be an ideal state from which it differs. Based on the above-described considerations we can state that any phenomenon and object in time and space is determined by a set of variables that are most likely not fully equilibrated. In certain circumstances when external forces are dramatically powerful, these minor variability components have little impact on the overall change of state observed. On the other hand, their impact within the boundaries of freedom is so tremendous that they do not make possible long-term predictions as a result of error multiplication during error propagation. If we have a deeper look at this distance from the predicted value of a model, we can see that it is the clear manifestation of the uniqueness in time and space of every moment, it is the footprint of time with its uniqueness and unrepeatability that makes life a series of unique events without a chance to repeat them. By this we can also claim that the term error in this context is erroneous as what we see is rather the footprint of time, the vibration of matter as a result of specific forces that affect the matter in that specific context.

Mathematical models have their stochastic components and these provide limits for long term predictability. Darwin described that selection is generating novel species by selecting organisms that fit better to a new change in the environment. Variability is the foundation of selection. Schrödinger pointed out that features are not changed in an analogue, continuous manner as they are encoded in the aperiodic crystals, which later was identified as the double helix of DNA. As a consequence, the code and the features encoded can change only in increments and not in a continuous manner. This turned inheritance into a set of boundaries, namely that all our properties are encoded in our DNA and as a result, our fate, together with all components of our behavior from our taste to our body weight and shape including our addictions and sexual orientation are encoded in our DNA. The cultural consequence of these observations was that we are not free, we are the output of our genes, we do not have any responsibility whatsoever. Epigenetics that started as a theory to describe the influx of information from the environment towards the genome, describes that tiny modifications on the DNA can modify the way how the code is interpreted (Nanney, "Epigenetic Control Systems."). Living organisms have a broad spectrum of features, much broader than the ones that could be explained by the genetic background. The DNA does not transmit the information in its pure state but in complex proteins, regulatory RNA molecules and ultimately by the whole cellular content of the sperm and egg. Some of these components are affecting the DNA sequence itself, some are affecting just the physical carriers of the DNA, namely the histones or tiny marks that are present in a covalent manner on DNA (e.g. DNA methylation, hydroxylation). All these modifications are changing the context of the DNA and, as a result, can change the output of the code carried by the DNA itself (Allis and Jenuwein, "The Molecular Hallmarks"). Moreover, systematic gene knock-out experiments highlighted that features are not always encoded on the level of individual genes but more likely in pathways (Barbaric, Miller, and Dear, "Appearances"). In a living organism, there is an abundance in alternative pathways that can have a combined effect on the manifestation of a genetic feature. As a summary, we can state that the fertilized egg will generate one unique and irreproducible organism that is the sum of both deterministic, environmental and stochastic events.

Uniqueness in time is the current immediate difference from anything that could be predicted. Besides the big comfort that we can gain from this knowledge, we can also see the fragility of life. Life is in all aspects particular and unique, with an open interpretation framework as the DNA code itself, where nucleotide triplets have an encoded wobbling. From the three nucleotides that code for an amino acid, during translation in the ribosomes, only two nucleotides bind strongly to the RNA and the third element of the code is wobbling. This allows variability in our DNA that is not present on protein levels. By studying the stochastic components of single-cell regulation, we can also see that in biological complex systems output is depending on a series of individual components that have their own error rates (Blake et al., "Noise"). This flexibility can be exploited by novel drugs that aim to overcome the premature stop codons that cause genetic diseases. Error generating drugs can be used to overcome translation stop signals in the genome and to produce healthy proteins in the genetically diseased patient. Error inducing agents can be used to modulate what seemed previously a fully deterministic genetic disease (Keeling et al., "Suppression"; Bidou et al., "Sense from Nonsense"). In these cases, an error-inducing drug cures disease by inducing errors in the reading of an erroneous code making the sum of errors to generate correct output. These observations enforce the approach that the code itself allows variability and as the code is carried by molecules on physical substrates the statistic deterministic variability is present on this level too. All these levels of variability bring us back to the ability of life to adapt to specific environmental changes. Nothing is fully deterministic in living systems, they have a spectacular space for individual variability. We are not operating in a deterministic framework, which allows us tremendous freedom but also gives us immense fragility.

The opportunity to act, to correct, to change the current state of a system by an individual that is part of the described system was addressed in economics by the Theory of Reflexivity by George Soros (Soros, "Fallibility"; Soros, "General Theory"). In the Theory of Reflexivity, the interpretations of a current economic, social or any situation or state that has a significant subjective component tend to dissociate from the original value propositions and distort the perceptions of the particular events. These distortions will lead to erroneous interpretations and inherently to over- or underestimations of the values of companies or national currencies. In this situation the dominant narratives, the overall used models start to control the behavior of several players of a field, or in the worst case the behavior of masses. The perception of value is extrapolated in the mathematical model and the assumptions of that particular model. Being ruled by these models (from stock exchange assumptions to peer pressure and fashion) is definitely a limitation of our freedom and corrections to the attributed value to real value triggered by individual decisions brings us back into the genuine state of controlling our own decisions, to the state of freedom. The story of stock exchange fortunes (e.g the story of George Soros' wealth) shows that such corrections lead not only to a subjective feeling of freedom but also to a real accumulation of freedom in the form of wealth.

The opportunity of the self to act against general perceptions of the environment is definitely a manifestation of freedom. These acts of freedom are rewarding us not only on the psychological level but can change our overall reality. If entropy, the final force of all destructive powers is causing general decay of system, all our individual decisions that act independently of the general assumptions will change our reality and will further open novel opportunities. Our decisions to change how we react in certain situations is adding novel levels of the error to any model that aims to describe us. These opportunities for non-deterministic decisions are rooted in the non-repeatability of each and every individual moment complemented with the ability to have a presence of the self, an understanding of the entropy of each moment and of the degrees of freedom of that particular moment. The state of mind that allows us not to follow general patterns but change these patterns is rooted in the state of "being present".

So what is freedom? We perceive freedom as the opportunity to select between different choices and slavery as the complete opposite of freedom when our choices are minimal and our tasks are determined from outside. By understanding the uniqueness in time of each and every individual moment and by merging this unique opportunity with our degrees of freedom, we reach a novel state of being present – the so much applauded mindfulness (Academic Mindfulness Interest Group and Academic Mindfulness Interest Group, "Mindfulness-Based Psychotherapies"; Langer and Ngnoumen, "Mindfulness."). Being present in a mindful state can change our perspective of being part of a "population" that can be described with the stochastic-deterministic models of statistical approaches to the perspective of having endless opportunities in each individual moment, opportunities that provide us a much larger degree of freedom compared to the obvious opportunities identified by a superficial assessment of the situation.

In trying to change our present situation, our attention can shift from being present into focusing on detecting the boundaries of freedom. We feel attacked if any external force is limiting our choices and we rejoice once our freedom is enlarged. News and journalism are monitoring the events that are challenging the boundaries of freedom. Both widening or restricting our freedom by any means is worth sharing with our fellows. Any act that is widening the limits of freedom is an act that is remembered by the community living within those limits. Social justice, going to the Moon, breaking a speed limit or a technological breakthrough is relevant as much as it is resetting our freedom of choice. Science and technology are about widening our space where we can make future plans. The "sharing economy" reached significant success as it opened up a large pool of opportunities for many that had no access to these choices. Conquering a new pike of a mountain made it accessible for the many and was a unique event in history. Challenging any previous limit is worth the attention of the whole community affected by that limit. What we still lack is the increase in the understanding of the individual person. Our lives are much more affected by our own beliefs in our own personal boundaries and limits and much less by the overall limitations of our communities.

But do wider opportunities really increase freedom? Being able to reach the moon or climb the Everest means that this would be a true choice for all and should be considered as an opportunity within the space of choices? How does the space of opportunities change the space of responsibility? Based on the stochastic-deterministic approach to nature and the widening of the error space of the models that rule our life we can affirm that understanding the atomic-molecular basis of our own freedom and the uniqueness of each moment in time is definitely shifting our life from a full deterministic view to a view of full responsibility. It is not the genes that determine our choices, and our freedom is much wider than we are willing to accept. Genes might be limiting to break world records in sports but it is fully our own responsibility to build our muscles by regular training. The deterministic components of our life become relevant when we reach the real limits. Within these limits, we have tremendous freedom described very well by statistical approaches. The fact that we do not live by our freedom is that we limit ourselves by narrow learned models. Being present and understanding the uniqueness of the moment can open-up the gates of freedom. We live by our own models in our own space of freedom, called also comfort zone, but this space is more cultural-psychological than genetic or biological. We are bound by these models that we learned during our personal life or as a society and we admit some minor flexibility within these models. Real freedom is in our decision to not follow the models that rule our life, in understanding the space of freedom that cannot be ruled by any mathematical model and in starting to live within our real biological-physical boundaries. The work we all need to do is to get rid of our enslaving models and start enjoying each and every moment of the present as unique moments of freedom that will never be the same in the future and have a unique opportunity to make decisions that are rooted in our unique self. Beyond being present, we propose a novel attitude towards unpredictability of mathematical models, namely to shift our attention from error and failure of the models towards the inherent freedom of this uncertainty component.

Works cited

Academic Mindfulness Interest Group, Melbourne and Melbourne Academic Mindfulness Interest Group. "Mindfulness-Based Psychotherapies: A Review of Conceptual Foundations, Empirical Evidence and Practical Considerations." *Australian & New Zealand Journal of Psychiatry* 40.4 (2006):285–94.

Allis, C. David and Thomas Jenuwein. "The Molecular Hallmarks of Epigenetic Control." *Nature Reviews Genetics* 17.8 (2016):487–500.

Barbaric, I., G. Miller, and T. N. Dear. "Appearances Can Be Deceiving: Phenotypes of Knockout Mice." *Briefings in Functional Genomics and Proteomics* 6.2 (2007): 91–103.

Bidou, Laure, Valérie Allamand, Jean Pierre Rousset, and Olivier Namy. "Sense from Nonsense: Therapies for Premature Stop Codon Diseases." *Trends in Molecular Medicine* 18.11 (2012): 679–88.

Blake, William J., Mads Kærn, Charles R. Cantor, and J. J. Collins. "Noise in Eukaryotic Gene Expression." *Nature* 422.6932 (2003): 633–37.

Cen, Ming and Daisheng Luo. "Error-Space Estimation Method and Simplified Algorithm for Space Target Tracking." *Applied Optics* 49.28 (2010): 5384–90.

Fisher, Moria E., Felix C. Huang, Zachary A. Wright, and James L. Patton. 2014. "Distributions in the Error Space: Goal-Directed Movements Described in Time and State-Space Representations." Pp. 6953–56 in *2014 36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBC 2014*. Institute of Electrical and Electronics Engineers Inc.

Gaspard, Pierre and Xiao Jing Wang. "Noise, Chaos, and (ε, τ)-Entropy per Unit Time." *Physics Reports* 235. 6 (1993): 291–343.

Gödel, Kurt. "Über Formal Unentscheidbare Sätze Der Principia Mathematica Und Verwandter Systeme I." *Monatshefte Für Mathematik Und Physik* 38.1 (1931): 173–98.

Halliwell, J. J. (Jonathan J. .., J. Pérez-Mercader, and Wojciech Hubert Zurek. *Physical Origins of Time Asymmetry*. Cambridge University Press, 1996.

James, Gareth, Daniela Witten, Trevor Hastie, and Robert Tibishirani. *An Introduction to Statistical Learning with Applications in R (Older Version)*. 2013.

Janson, Lucas, William Fithian, and Trevor J. Hastie. "Miscellanea: Effective Degrees of Freedom: A Flawed Metaphor." *Biometrika* 102.2 (2015): 479–85.

Keeling, Kim M., Dan Wang, Sara E. Conard, and David M. Bedwell. "Suppression of Premature Termination Codons as a Therapeutic Approach." *Critical Reviews in Biochemistry and Molecular Biology* 47.5 (2012): 444–63.

Langer, Ellen J. and Christelle T. Ngnoumen. "Mindfulness." Pp. 95–111 in *Positive Psychology*. Routledge, 2018.

Nanney, D. L.. "Epigenetic Control Systems." *Proceedings of the National Academy of Sciences* 44.7 (1958):712–17.

Ozgyin, Lilla, Attila Horvath, Zsuzsanna Hevessy, and Balint L. Balint. "Extensive Epigenetic and Transcriptomic Variability between Genetically Identical Human B-Lymphoblastoid Cells with Implications in Pharmacogenomics Research." *Scientific Reports* 9.1 (2019): 4889.

Pandey, Shanta and Charlotte Lyn Bright. "What Are Degrees of Freedom?" *Social Work Research* 32 (2008):119–28.

Schrödinger, Erwin. "What Is Life?: The Physical Aspect of the Living Cell; with Mind and Matter; & Autobiographical Sketches." *Mind and Matter*. 1992.

Soros, George. “Fallibility, Reflexivity, and the Human Uncertainty Principle.” *Journal of Economic Methodology* 20.4 (2013): 309–29.
Soros, George. “Soros: General Theory of Reflexivity.” *Financial Times* 2014. 1–6.
Swanton, Charles and Stephan Beck. “Previews Epigenetic Noise Fuels Cancer Evolution.” *Cancer Cell* 26.6 (2014): 775–76.
Varotsos, P. A., N. V. Sarlis, H. K. Tanaka, and E. S. Skordas.. “Some Properties of the Entropy in the Natural Time.” *Physical Review E - Statistical, Nonlinear, and Soft Matter Physics* 71.3 (2005).

Author’s profile:

Balint L. Balint teaches Biochemistry, Molecular Biology and Genomics in the Department of Biochemistry and Molecular Biology of the Medical Faculty at the University of Debrecen, Hungary. His primary research interests are the interference between genomics and epigenomics, the impact of the stochastic events and the personal genome to the biological responses observed in human cells. He has made a significant contribution to the better understanding of how super-enhancers of the genome are assembled upon hormonal stimuli. Email: balintblaszlo@gmail.com and lbalint@med.unideb.hu. ORCID profile: https://orcid.org/0000-0002-6163-7190