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Editorial Article

Information theory of non-equilibrium states

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Abstract – The Shannon's information theory of equilibrium states has already underpinned fundamental progress in a diverse range of subjects such as computing, cryptography, telecommunications, physiology, linguistics, biochemical signaling, mathematics and physics. Here we undertake a brief examination of the concept of information theory of non-equilibrium states. The fundamental approach proposed here has the potential to enable new applications, research methods and long-term innovations, including the principle of extracting digital information from non-equilibrium states and the development of predictive protocols of mutation dynamics in genome sequences.

Keywords – non-equilibrium information theory; thermal fluctuations; digital bits; information entropy;

1. Introduction

Information is a very abstract entity that comes in many forms including analogue information, biologically encoded DNA / RNA information, quantum information and digital information. Shannon developed the classical information theory in 1948 [1] and he is considered one of the main contributors to modern computing, as well as the inventor of the unit of information, "bit". Shannon's information theory is based on the mathematical formulation of the amount of information extracted from observing the occurrence of an event. Using an axiomatic approach, he defined information (I) extracted from observing an event as a logarithmic function of the probability (P) of the event to occur or not, $I(P) = -\log_b P = \log_b(1/P)$, where the base b gives the units of information, so for binary bits, $b = 2$. For a set of U independent and distinctive events $X = \{x_1, x_2, \ldots, x_U\}$, a probability distribution $P = \{P_1, P_2, \ldots, P_U\}$ on X could be defined, so that each event x_j has a probability of occurring $P_j = P(x_j)$, where $P_j \geq 0$ and $\sum_{j=1}^{U} P_j = 1$.

According to Shannon, the average information extracted per event, or the number of bits of information per event, when observing the set X once is:

$$H = -\sum_{j=1}^{U} P_j \cdot \log_b P_j \tag{1}$$

The function H resembles an information entropy function and it is maximum when the events x_j have equal probabilities of occurring, $P_j = 1/U$, so $H = \log_b U$. When observing N sets of events X, or equivalently observing N times the set of events X, the number of bits of information extracted from the observation is the product $N \cdot H$.

Let us assume a two state physical system that could be used as a digital bit memory cell to store information. For this specific case of digital information, $b = 2$, and there are two possible distinctive events / states, $U = 2$ and $X = \{0,1\}$. If the system is at equilibrium, and assuming no biasing or external work on the system, then the two events / states

have equal probabilities of occurring, $P_j = 1/U = 1/2$ so $P = \{P_0, P_1\} = \{1/2, 1/2\}$, and it can be shown that $H = \log_2 2 = 1$. The meaning of $H = 1$ is that observing the above event generates 1 bit of information.
For a set of N such sates, we can link information theory to thermodynamics, as the number of possible states, also known as distinct messages in Shannon's original formalism, is equivalent to the number of information bearing microstates, Ω, compatible with the macro-state [2]:

$$\Omega = 2^{N \cdot H} \tag{2}$$

Using (1) and (2), the entropy of the information bearing states, using Boltzmann thermodynamic entropy, can be defined as [2]:

$$S = k_b \cdot \ln(\Omega) = N \cdot k_b \cdot H \cdot \ln(2) \tag{3}$$

where $k_b = 1.38064 \times 10^{-23}$ J/K is the Boltzmann constant.

However, Shannon's theory ignores any particular features of the event, the observer, or the observation method. The most important assumption is that the observed events are at equilibrium and are therefore described by their time independent equilibrium probabilities, P_j. However, real physical systems consist of microstates undergoing transitions from one microstate to another, even when a system is isolated, or at thermal equilibrium. Unlike Shannon's time independent equilibrium probabilities, P_j, these processes are described by non-equilibrium time dependent probabilities, $P_j(t)$.

Here we take a novel approach by re-formulating the Shannon's information theory for non-equilibrium states. The key aspect here is to describe the observed events and their associated states using non-equilibrium time dependent probabilities. This will produce an information entropy function that is time dependent, so the information extracted from observing such events is also time dependent. This theoretical approach has profound implications with transformative potential, enabling further applications of the information theory to a very diverse range of new science and technology areas. To demonstrate the capability and the potential of this fundamental work, we will discuss briefly how this theory could be used to facilitate two important applications.

2. Non-equilibrium statistics

In order to develop the information theory of non-equilibrium states, the key approach is to recognize that the non-equilibrium states are simultaneously the observed "events" in Shannon's information theory, and also the microstates (j) described by the probability distribution P_j that a given macro system is in one of the possible microstates (j). The evolutions of these non-equilibrium microstates are described by the non-equilibrium statistics, in which their non-equilibrium probabilities are time dependent, $P_j(t)$. The time evolution of the probabilities when a non-equilibrium system goes through different possible states are described by the Pauli-Master equation [3]:

$$\frac{dP_j(t)}{dt} = \sum_{m \neq j} \left(a_{j,m} P_m(t) - a_{m,j} P_j(t) \right) \tag{4}$$

where: $1 \leq j,m \leq \Omega$ with j and m taking integer values and Ω is the number of possible states of the system (i.e. number of microstates compatible with the macro-state). $P_j(t)$ and $P_m(t)$ are the probabilities that the system is in the state j or m at the time t, respectively. $a_{j,m}$ and $a_{m,j}$ are the transition rates per unit time from the state m to state j and vice versa, respectively. The equation (4) is in fact a system of Ω differential equations and the general solution can be formulated analytically for: a) an isolated system; b) a system in contact with a temperature reservoir.
The coefficients $a_{j,m}$ and $a_{m,j}$ are also positive and time independent. For an isolated system, the transition rates per unit time link transitions between states (j) and (m) having the same energy, satisfy the symmetry relation:

$$a_{j,m} = a_{m,j} \tag{5}$$

For a system in contact with a thermal reservoir (i.e. canonical ensemble), the transition rates can link states (j) and (m) having different energies and satisfying the pseudo-symmetry relation between the transition rates:

$$a_{j,m}e^{-\left(\frac{W_m}{k_b T}\right)} = a_{m,j}e^{-\left(\frac{W_j}{k_b T}\right)} = \upsilon_0 \tag{6}$$

where W_m and W_j are the energies in the state m and j, respectively, k_bT is the thermal energy and v_0 is a constant equal to the total number of trials per second to overcome the energy barrier.

3. Non-equilibrium probabilities of digital states

Let us assume a two state physical system that could be used as a digital bit memory cell to store information. We can then assign at equilibrium the digital logical state "0" to state m and the logical state "1" to state j. Let us assume that the two stable states of the system have equal energies, $W_1 = W_0 = -W_b$, where W_b is the energy barrier (see figure 1). Without any external perturbations, the system will maintain its state indefinitely and two states are equally probable. Taking, U = 0,1 and b = 2, Shannon theory gives the information content extracted from observing this physical system as equal to 1 bit per observation (see relation (1)):

$$H = -P_1 \cdot \log_2 P_1 - (1-P_1)\cdot \log_2(1-P_1) \tag{7}$$

where we used in (1) and (7) the normalization condition, $P_1 + P_0 = 1$.

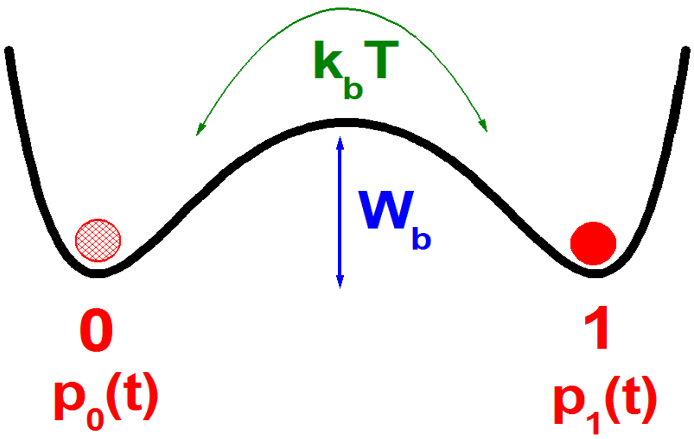

Figure 1. Two state – 1 bit memory system thermally unstable.

We are now examining the case in which the system is not at equilibrium and jumps between states 0 and 1 occur randomly at a given rate due to various effects such as thermal activation, external perturbative fields, and so on. In this case, the probabilities that the system is in state 0 or state 1 are no longer constant and they are in fact time dependent. In order to investigate this special non-equilibrium information case, we now particularize the Pauli-Mater equation (4) for a two state system, in contact with a thermal reservoir. For $j,m = 0,1$ and using relations (4) and (6), the Pauli-Master equation becomes a system of two differential equations:

$$\begin{cases} \frac{dP_1}{dt} = a_{1,1}P_1 + a_{1,0}P_0 = \upsilon_0\left(-P_1 e^{\frac{W_1}{k_B T}} + P_0 e^{\frac{W_0}{k_B T}}\right) \\ \frac{dP_0}{dt} = a_{0,1}P_1 + a_{0,0}P_0 = \upsilon_0\left(P_1 e^{\frac{W_1}{k_B T}} - P_0 e^{\frac{W_0}{k_B T}}\right) \end{cases} \tag{8}$$

Solving (8) we obtain the following time dependent probabilities:

$$P_1(t) = C_1 + C_2 \cdot e^{-\left(\frac{t}{\tau}\right)} \tag{9}$$

$$P_0(t) = C_1 \cdot e^{\frac{W_1 - W_0}{k_b T}} - C_2 e^{-\left(\frac{t}{\tau}\right)} \tag{10}$$

where C_1 and C_2 are constants to be determined. $W_1 - W_0 = 0$ in the absence of any perturbative fields, and τ is the relaxation time of the system:

$$\tau^{-1} = \upsilon_0 \cdot \left(e^{\frac{W_1}{k_b T}} + e^{\frac{W_0}{k_b T}} \right) = 2\upsilon_0 \cdot e^{-\left(\frac{W_B}{k_b T}\right)} \tag{11}$$

This represents the relaxation time of the system in the absence of any perturbations, in response to thermal activation, which in our case results in memory switching. The meaning of this relaxation time is the mean time between spontaneous memory transitions under the thermal activation. Constants C_1 and C_2 can be determined from the initial and final conditions in conjunction with the normalization condition. Hence, imposing $t = 0$ (initial condition), then relation (9) becomes:

$$P_1(0) = C_1 + C_2 \tag{12}$$

Imposing $t \rightarrow \infty$ where the system tends to equilibrium, relations (9) and (10) become:

$$P_1(\infty) = P^1{}_{eq} = C_1 \tag{13}$$

$$P_0(\infty) = P^0{}_{eq} = C_1 \cdot e^{\frac{W_1 - W_0}{k_b T}} \tag{14}$$

However, from the normalization condition we have: $P_1(\infty) + P_0(\infty) = 1$, which combined with relations (13) – (14) results in:

$$C_1 = P^1{}_{eq} = \left(1 + e^{\frac{W_1 - W_0}{k_b T}} \right)^{-1} \tag{15}$$

From (12) we have:

$$C_2 = P_1(0) - C_1 = P_1(0) - P^1{}_{eq} \tag{16}$$

Having the two constants determined, the occupation probabilities (9), (10) can be written as:

$$P_1(t) = P_1(0) \cdot e^{-\left(\frac{t}{\tau}\right)} + P^1{}_{eq} \cdot \left(1 - e^{-\left(\frac{t}{\tau}\right)} \right) \tag{17}$$

$$P_0(t) = \left(1 - P^1{}_{eq}\right) + \left(P^1{}_{eq} - P_1(0)\right) \cdot e^{-\left(\frac{t}{\tau}\right)} \tag{18}$$

For our special case when no external forces or perturbations are acting on the system, so $W_1 - W_0 = 0$, then from (15), $P^1{}_{eq} = 1 / 2$ and the new probabilities are:

$$P_1(t) = P_1(0) \cdot e^{-\left(\frac{t}{\tau}\right)} + \frac{1}{2} \cdot \left(1 - e^{-\left(\frac{t}{\tau}\right)} \right) \tag{19}$$

$$P_0(t) = \frac{1}{2} + \left(\frac{1}{2} - P_1(0)\right) \cdot e^{-\left(\frac{t}{\tau}\right)} \tag{20}$$

As seen from relations (19) and (20), in order to determine the occupation probabilities for the states 1 and 0, one needs to have a precise knowledge of the initial occupation probability of the state *1* at $t = 0$, $P_1(0)$. The initial conditions of the system depend in turn on the history of the experiment. Therefore, a comparison between the memory dynamics of the same system during different observations is relevant only if the system has been reset back to the same initial conditions before each observation. In this work we assume for example that the memory state has been initially set into state 1, so that $P_1(0) = 1$. Using the imposed initial state $P_1(0) = 1$, relations (19) and (20) become:

$$P_1(t) = e^{-\left(\frac{t}{\tau}\right)} + \frac{1}{2} \cdot \left(1 - e^{-\left(\frac{t}{\tau}\right)}\right) \tag{21}$$

$$P_0(t) = \frac{1}{2} \cdot \left(1 - e^{-\left(\frac{t}{\tau}\right)}\right) \tag{22}$$

and they give a full temporal description of the occupation probability of the two possible memory states. For N memory states, we define $N_1(t) = P_1(t) \cdot N$ as the number of sites in state 1 at time t and $N_0(t) = P_0(t) \cdot N$ the number of sites in state 0 at time t, with $N = N_1 + N_0$.

4. Non-equilibrium Shannon information entropy

Solving Pauli-Master equation for the special case of two state system gave us analytical solutions for $P_1(t)$ *and* $P_0(t)$. These solutions can then be combined with Shannon's information theory to derive interesting results concerning the information content of non-equilibrium states. Observing a non-equilibrium system on timescales comparable to the relaxation time (τ) of the system, $t \sim \tau$, will generate a very abstract entity, namely the general expression of the time dependent Shannon information entropy, $H(t)$:

$$H(t) = -\sum_{j=1}^{\Omega} P_j(t) \cdot \log_b P_j(t) \tag{23}$$

Hence, equilibrium states are in fact particular solutions of the Pauli-Master equation for non-equilibrium systems, so that $P_j(t) \rightarrow P_j$ when the observation time is either much shorter ($t << \tau$), or much longer ($t \rightarrow \propto$) than the characteristic relaxation time. For the particular case of digital states, this becomes:

$$H(t) = -P_1(t) \cdot \log_2 P_1(t) - (1 - P_1(t)) \cdot \log_2 (1 - P_1(t)) \tag{24}$$

where $P_1(t)$ is given by (21), P^1_{eq} is given by (15) and the relaxation time is given by (11).
Using this theory, one could examine possible applications by selecting and studying theoretically two interesting non-equilibrium systems: a) system with very short relaxation times ($\tau < 10^{-6}$ *s*); b) system with very long relaxation times ($\tau > 10^5$ *s*) relaxation times.

5. Possible applications

5.1. Extraction of digital information from non-equilibrium states ($\tau < 10^{-6}$ s)

The global need for digital data storage is increasing exponentially. IBM estimates that 2.5 billion Gigabytes of digital data are produced every day on Earth [4,5]. This huge digital data production demands development of new storage technologies that meet the increasing demand. Regardless of the storage technology used (magnetic, solid-state, optical), the increased data density is universally achieved by shrinking the physical bit size. However, this cannot be sustained indefinitely due to physical limitations that render the information bit thermally unstable, when it becomes smaller than a critical bit size (examples: super-paramagnetic limit, thermal charge diffusion limit, etc). If the current growth rate in data storage densities is to continue, new ways of dealing with these thermal instabilities should be identified. The novel approach proposed here to extract information from non-equilibrium states is a possible solution that makes the current efforts to improve the bit thermal stability limits futile. Instead, one could use the non-equilibrium information theory for processes of short relaxation time ($\tau < 10^{-6}\, s$) to formulate the theoretical framework and to define the protocol of extracting information directly from non-equilibrium thermally unstable information bits.

We hope this work will stimulate further research and development to identify possible mechanisms by which digital information could be extracted from these non-equilibrium states. The main output would be a framework that would allow further physical shrinking of the digital bit size to beyond the current *state-of-the-art*, facilitating unprecedented digital data storage densities in the future.

5.2. *Dynamics of genome mutations using non-equilibrium information theory* ($\tau > 10^5$)

Using the information theory to study genome sequences is not new [6-18]. However, the approach proposed here enables new avenues for research in the field of bio-informatics. Thinking of the genome as a coding system, it is possible to use Shannon's information theory to analyze interesting sections of a genome and to map its information entropy spectrum [19]. In this way, one can corroborate special features in the information entropy spectrum to interesting and significant aspects of the genome, including the inflection points where known mutations occurred.

DNA / RNA genomes are information systems that store biological information. They consist of a very large string of A, C, G, and T letters, which stand for the nucleotides: adenine (A), cytosine (C), guanine (G), and thymine (T) (or uracil (U) replacing T in RNA). Let us consider a DNA subset randomly generated, consisting of $N = 34$ letters, and a mutated version of the same genome subset (see Figure 2):

CACTTATCATTCTGACTGCTACGGGCAATATGTG - Original subset

↓

CACTTATCATACTGACTGCTACGGGCAATATGTG - Mutated subset

Figure 2. Example of a single base point genome mutation (T into A).

Applying the information theory, our set of independent and distinctive events becomes $X = \{A, C, G, T\}$, so $U = 4$ and probabilities $P = \{P_A, P_C, P_G, P_T\}$. Using digital bits, $b = 2$, for $U = 4$ we need 2 bits per letter, $H = \log_b U = 2$ to encode the message: $A = 00$, $C = 01$, $G = 10$, $T = 11$. If the letters within this subset would have equal probabilities to occur (1/4), then the subset would have $H = 2$ and a total entropy of $NH = 68$ bits of information. However, the original subset has the following probability distribution and information entropy:

$$P = \left\{ P_A = \frac{8}{34}, P_C = \frac{8}{34}, P_G = \frac{7}{34}, P_T = \frac{11}{34} \right\} \qquad H_{original} = -\left(\frac{8}{34}\log_2\left(\frac{8}{34}\right) + \frac{8}{34}\log_2\left(\frac{8}{34}\right) + \frac{7}{34}\log_2\left(\frac{7}{34}\right) + \frac{11}{34}\log_2\left(\frac{11}{34}\right) \right) = 1.978$$

Therefore, the information entropy of the original subset is 1.978 bits and the total information encoded is 67.25 bits. The mutated subset has the following probability distribution and information entropy:

$$P = \left\{ P_A = \frac{9}{34}, P_C = \frac{8}{34}, P_G = \frac{7}{34}, P_T = \frac{10}{34} \right\} \qquad H_{mutated} = -\left(\frac{9}{34}\log_2\left(\frac{9}{34}\right) + \frac{8}{34}\log_2\left(\frac{8}{34}\right) + \frac{7}{34}\log_2\left(\frac{7}{34}\right) + \frac{10}{34}\log_2\left(\frac{10}{34}\right) \right) = 1.987$$

The information entropy of the mutated genome subset is 1.987 bits, and the total information encoded is 67.55 bits. Hence, the information entropy difference between the original and mutated subsets is $\Delta H = 0.009$ bits and the difference in the total information encoded is 0.306 bits. This demonstrates the concept of using the information theory to study genetic mutations.

By applying this technique to a known genome and its mutated version, a calibration protocol could enable this procedure to be utilized in reverse, as a predictor of future genetic mutations [20], especially when combined with the second law of information dynamics [21].

However, a full predictive algorithm of genetic mutations can only be achieved when genetic mutations are regarded as non-equilibrium processes of long relaxation time ($\tau > 10^5\, s$). In this framework, the non-equilibrium statistics combined with the information theory and the second law of information dynamics could fully describe the dynamics of genetic mutations. Hence, the information theory of non-equilibrium states will enable truly transformative advances in medicine, genetics, virology, evolution theory and bio-informatics. The only complexity in terms of genomic sequences is the fact that these are no longer two state information systems like the digital states. Instead they are 4-state systems containing the A, C, G, and T letters. Solving Pauli-Master equation for a non-equilibrium 4-state system is possible, but significantly more complicated, especially when analytical solutions are required.

6. Conclusions

In this article we combined the classical Shannon's information theory with non-equilibrium statistics to derive analytical expressions of the non-equilibrium information entropy and information content of non-equilibrium states. Using this theory, one could envisage a range of possible applications, depending on the relaxation times of the processes involved. Here we proposed a mechanism that could facilitate extraction of information from unstable digital bits / states when the relaxation times are in the range $\tau < 10\text{-}6$ s. We also explained the methodology afforded by the information theory to study genetic mutations. When this is combined with the non-equilibrium statistics and the second law of information dynamics, a possible protocol for predicting genetic mutations in bio-systems with long relaxation times $\tau > 105$ s, could emerge. The current consensus is that genetic mutations are random processes [22], but recent studies demonstrated that a hidden information entropic force and the second law of information dynamics in fact drive the genetic mutations [20,21].

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References

[1] C.E. Shannon, A mathematical theory of communication, The Bell System Technical Journal, Vol. 27, pp. 379–423 (1948).
[2] M.M. Vopson, The mass-energy-information equivalence principle, AIP Adv. 9, 095206 (2019).
[3] H. J. Kreuzer, Nonequilibrium Thermodynamics and Its Statistical Foundations (Oxford University Press, Oxford, 1981)
[4] P. Zikopoulos, D. deRoos, K. Parasuraman, T. Deutsch, J. Giles, and D. Corrigan, Harness the Power of Big Data: The IBM Big Data Platform (McGraw-Hill Professional, New York, 2012), ISBN: 978-0-07180818-7.
[5] M. M. Vopson, The information catastrophe, AIP Adv. 10, 085014 (2020).
[6] T.A. Reichert, D.N. Cohen, A.K.C. Wong, An application of information theory to genetic mutations and the matching of polypeptide sequences, J. Theoret. Biol. 42, 245-261 (1973).
[7] C.Cosmi, V. Cuomo, M. Ragosta, M.F. Macchiato, Characterization of nucleotide sequences using maximum entropy techniques, J. Theoret. Biol. 147, 423-432 (1990).
[8] H. Herzel, W. Ebeling, A.O. Schmitt, Entropies of biosequences: The role of repeats, Phys. Rev. E 50, 5061-5071 (1994).
[9] W. Li, K. Kaneko, Long-range correlations and partial 1/f spectrum in a noncoding DNA sequence, Europhys. Lett. 17(7), 655-660 (1992).
[10] C.K. Peng, S.V. Buldyrev, A.L. Goldberger, S. Havlin, F. Sciortino, M. Simon, H.E. Stanley, Long-range correlations in nucleotide sequences, Nature 356, 168-170 (1992).

[11] L. Wentian, G.M. Thomas, K. Kunihiko, Understanding long-range correlations in DNA sequences, Physica D: Nonlinear Phenomena, Volume 75, Issues 1–3, 392-416 (1994) https://doi.org/10.1016/0167-2789(94)90294-1.
[12] R. Roman-Roldan, P. Bernaola-Galván, J. Oliver, Application of information theory to DNA sequence analysis: A review, Pattern Recognition, Volume 29, Issue 7, (1996) https://doi.org/10.1016/0031-3203(95)00145-X.
[13] A. Hariri, B. Weber, J. Olmsted III, On the validity of Shannon-information calculations for molecular biological sequences, J. Theoret. Biol. 147, 235-254 (1988).
[14] S. Vinga, Information theory applications for biological sequence analysis, Briefings in Bioinformatics, vol. 15 (3) 376-389 (2014).
[15] J. A. Tenreiro Machado, Shannon Entropy Analysis of the Genome Code, Mathematical Problems in Engineering, Article ID 132625 (2012) https://doi.org/10.1155/2012/132625
[16] F. Fernandes, A.T. Freitas, J.S. Almeida, S. Vinga, Entropic Profiler – detection of conservation in genomes using information theory, BMC Research Notes, 2:72 (2009) doi:10.1186/1756-0500-2-72
[17] J.A. Tenreiro Machado, António C. Costa, Maria Dulce Quelhas, Shannon, Rényie and Tsallis entropy analysis of DNA using phase plane, Nonlinear Analysis: Real World Applications, Volume 12, Issue 6, 3135-3144 (2011) https://doi.org/10.1016/j.nonrwa.2011.05.013.
[18] A. Thomas, S. Barriere, L. Broseus, J. Brooke, C. Lorenzi, J.P. Villemin, G. Beurier, R. Sabatier, C. Reynes, A. Mancheron, W. Ritchie, GECKO is a genetic algorithm to classify and explore high throughput sequencing data, Commun. Biol. 2, 222 (2019). https://doi.org/10.1038/s42003-019-0456-9
[19] M. Vopson, S.C. Robson, A new method to study genome mutations using the information entropy, Physica A: Statistical Mechanics and its Applications, Volume 584, 126383 (2021).
[20] M.M. Vopson, A Possible Information Entropic Law of Genetic Mutations. *Appl. Sci.* 2022, *12*, 6912. https://doi.org/10.3390/app12146912
[21] M.M. Vopson, S. Lepadatu, The second law of information dynamics, in-press AIP Advances, vol. 12, issue 7 July (2022).
[22] Futuyma, D.J. Evolutionary Biology, 2nd ed.; Sinauer: Sunderland, MA, USA, 1986.