ISSN: 2164-5388 Volume 12, Number 3, July 2022

Scientific Research Publishing

Open Journal of Biophysics

ISSN: 2164-5388

https://www.scirp.org/journal/ojbiphy

Journal Editorial Board

ISSN Print: 2164-5388 ISSN Online: 2164-5396
https://www.scirp.org/journal/ojbiphy

Scientific Research Publishing

Open Journal of Biophysics, 2022, 12, 165-171
https://www.scirp.org/journal/ojbiphy
ISSN Online: 2164-5396
ISSN Print: 2164-5388

Table of Contents

Volume 12 Number 3 July 2022

Open Journal of Biophysics (OJBIPHY)
Journal Information

SUBSCRIPTIONS

The *Open Journal of Biophysics* (Online at Scientific Research Publishing, https://www.scirp.org/) is published quarterly by Scientific Research Publishing, Inc., USA.

Subscription rates:
Print: $79 per issue.
To subscribe, please contact Journals Subscriptions Department, E-mail: sub@scirp.org

SERVICES

Advertisements
Advertisement Sales Department, E-mail: service@scirp.org

Reprints (minimum quantity 100 copies)
Reprints Co-ordinator, Scientific Research Publishing, Inc., USA.
E-mail: sub@scirp.org

COPYRIGHT

PRODUCTION INFORMATION

For manuscripts that have been accepted for publication, please contact:
E-mail: ojbiphy@scirp.org

Scientific Research Publishing

Open Journal of Biophysics, 2022, 12, 165-171
https://www.scirp.org/journal/ojbiphy
ISSN Online: 2164-5396
ISSN Print: 2164-5388

Understanding Model Independent Genetic Mutations through Trends in Increase in Entropy

Sage Copling, Maansi Srinivasan, Preet Sharma*

Non-Linear Science Research Group, Center for Theoretical Research, Midwestern State University, Wichita Falls, USA
Email: sagecopling@my.unt.edu, maansirs@utexas.edu, *preet.sharma@msutexas.edu

How to cite this paper: Copling, S., Srinivasan, M. and Sharma, P. (2022) Understanding Model Independent Genetic Mutations through Trends in Increase in Entropy. *Open Journal of Biophysics*, **12**, 165-171.
https://doi.org/10.4236/ojbiphy.2022.123007

Received: June 25, 2022
Accepted: July 28, 2022
Published: July 31, 2022

Abstract

Introduction: A mutation, in general, can be defined as a change in the genetic sequence. Mutations can be changes as small as the substitution of a single DNA building block, or nucleotide base, with another nucleotide base. There can be larger mutations which can affect many genes on a chromosome. In this study we have tried to understand a normal mutation and a failed mutation from the point of view of entropy. We have shown that the entropy range of a normal mutation is less compared to the entropy range of a failed mutation. In this article we have plotted the increase of entropy of both types of mutations mentioned above. **Statistical Physics of Partition Function and Entropy:** In this section we have used statistical physics to define the partition function of an ensemble. Based on the partition function we have expressed how to calculate physical quantities such as average energy and entropy. **Model Independent Mutation Entropy:** The entropy of all processes increases. This is true even for biological systems. We have shown the difference between the entropy of a successful mutation and a failed mutation. **Conclusion:** In conclusion we have shown how the entropy of a successful mutation differs from that of a failed mutation. This opens up future research opportunities where we can apply this to specific biological systems.

Keywords

Statistical Physics, Mutations, Entropy, Energy

1. Introduction

Genetic entropy can be defined as the genetic breakdown of living things. As biological processes and mishaps occur, genetic entropy increases while the relationships between living things in the body become increasingly more chaotic

and complex. Mutations occur when the body codes for the wrong gene in a DNA sequence, whether it be from the environmental factors such as UV Radiation, or intrinsic factors such as errors in DNA synthesis and replication. Genetic entropy increases when things become less ordered, while mutations are humanity's physical manifestation of less order, in that they cause an increase in complexity every time they occur. As a result, it seems clear that genetic mutations increase genetic entropy by increasing amounts of disorder. There seem to be two primary ways by which genetic mutations affect the genetic entropy of humans. The first effect of mutations on genetic entropy occurs at an individual level. This process of entropy, also called biosemiotic entropy, describes an "error or deviation from a healthy state." Crucially, cancer is an accurate representation of biosemiotic entropy. Error in genetic code builds onto more errors, as the corrosion of code causes deletions and insertions to become huge frameshifts, and the accumulation of these random mutations ultimately causes an error in the cell-cycle control mechanism. When the cell loses control over its control mechanisms, a cancerous tumor develops while blood and nutrients are drawn toward the growth. The biosemiotic entropy of humans increases over the course of people's lives, so by the end of a human's life, the cells have accumulated thousands of mutations, which ultimately causes problems like cancer. The second effect of mutations on entropy occurs on an evolutionary basis more so than it does on a population-wide basis. As researchers have made clear, genetic mutations can not be spread through populations of people, one person cannot give their neighbor Duchenne's Syndrome or Red-Green Color-Blindness. However, evolution dictates that mutations, can be passed on from one generation to the next. We know that mutations stack up over time in an individual, and genetic entropy thereby increases. As a result, a population over time will constantly increase its genetic entropy as more disorder occurs in a genome. Overall, it is clear that genetic entropy is constantly increasing in the world, as chaos causes more chaos.

In biology, mutations are defined as alterations to the sequence of nucleotides in genetic material, whether it be DNA, RNA, proteins, or cells [1] [2] [3]. UV and ionizing radiation, chemical mutagens, viruses (such as lentiviruses and adenovirus as used in vectors), copying errors, and hyper-mutation are just some of the methods by which mutations may occur.

In eukaryotic organisms with germ cells, or reproductive cells, there are two types of common mutations. The first type, germ line mutations, can be transmitted to offspring via reproductive cells. Alternatively somatic mutations, which involve somatic or body cells, can not be transmitted to offspring [3] [4].

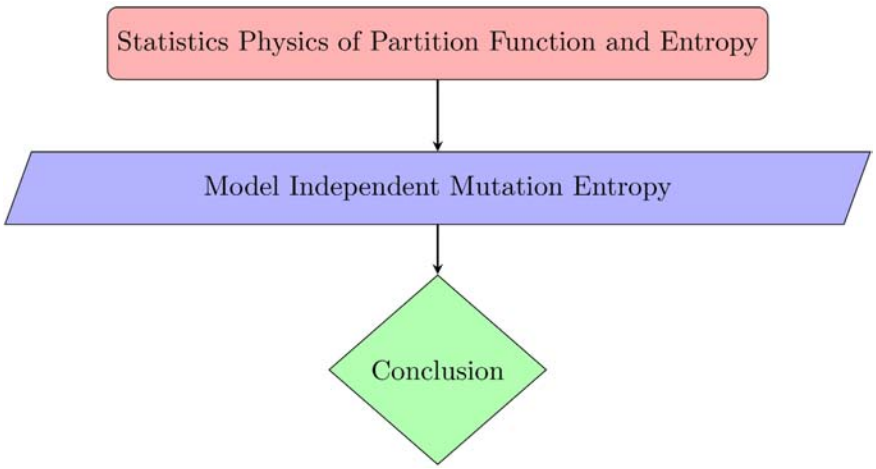
Asexual organisms often have different mechanisms of reproduction such as cuttings or budding, which can make the distinction between mutations become confusing. For example, some plants transmit somatic mutations in somatically mutated parts of plants where flower buds develop, which can be considered both asexual and sexual. Another mutation type is a de novo mutation, in which genetic mutations arise from DNA sequences that were not always meant to be

coded or undergo transcription and translation. While the source of these mutations is unrelated to the effects of the mutation, the type of cell may play a role in whether negative impacts occur.

Finally, in general, mutation is widely considered the mechanism upon which natural selection acts, causing advantageous genetic material and traits to multiply through survival, while causing disadvantageous genetic material and traits to reduce in quantity by dying out. As mentioned previously, the last important piece of information we mention in this paper is that mutations can be the result of inserted or deleted DNA through plasmids and vectors, different types of mobile genetic elements [5] [6] [7].

In this article we will study the statistical physics of model independent mutations. We will show that the entropy of a successful mutation and a failed mutation is different from the entropic aspects and the range in which the entropy of both types of mutations lie.

2. Organization of This Paper



3. Statistics Physics of Partition Function and Entropy

3.1. Partition Function

Partition functions describe the statistical properties of a system and are defined by functions of the thermodynamic state variables, such as the temperature and volume. Most of the thermodynamic variables of the system, such as the total energy, free energy, entropy, and pressure, can be expressed in terms of the partition function. Every partition function can be constructed in a way so that it represents a statistical ensemble.

The partition function can be defined as:

$$Z = \sum_i \exp^{-\beta E_i} \tag{3.1}$$

where $\beta = \frac{1}{k_B T}$, k_B is the Boltzmann constant and T is the temperature.

3.2. Average Energy

The average energy or the expectation value of the energy is given as:

$$\langle E \rangle = -\frac{\partial(\ln Z)}{\partial \beta} \tag{3.2}$$

Using Equation (3.1) we get

$$\langle E \rangle = k_B T^2 \frac{\partial(\ln Z)}{\partial T} \tag{3.3}$$

3.3. Variance in Energy

The variance in the energy of a system or the fluctuation in energy can be calculated by:

$$\left\langle (\Delta E)^2 \right\rangle = \left\langle \left(E - \langle E \rangle \right)^2 \right\rangle = \frac{\partial^2 (\ln Z)}{\partial \beta^2} \tag{3.4}$$

3.4. Entropy

The entropy is a thermodynamic quantity which is defined as the chaos in a system. It can be expressed with relation to the partition function as:

$$S = \frac{\partial}{\partial T}\left(k_B T (\ln Z)\right) \tag{3.5}$$

4. Model Independent Mutation Entropy

In this section we have used the temperatures and the average energies of a normal mutation as shown in Figure 1, and that of a failed mutation as shown in Figure 2. The energies have been scaled down to clearly express the ranges of entropies. The figures clearly indicate that the entropy range in a failed mutation is much higher compared to the entropy range in a normal mutation. The energies and the temperatures have been cited from [8] [9] [10] [11]. There are more

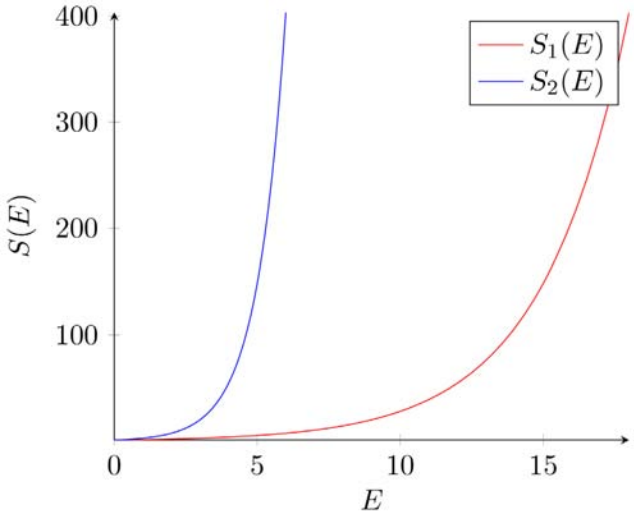


Figure 1. The entropy trends in a normal mutation.

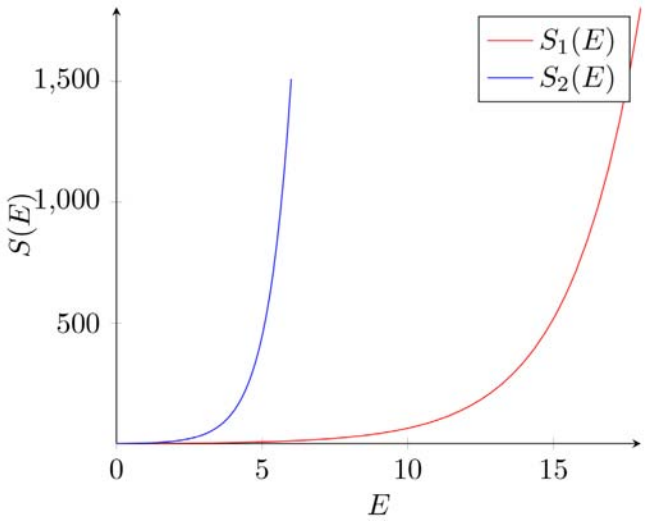


Figure 2. The entropy trends in a failed mutation.

studies which show detailed calculations of energies of very specific mutations [12] [13] [14] [15] [16]. We have limited our study to a general model independent approach. The graphs below show the plots of entropy vs energy in the cases of a normal mutation and a failed mutation.

In both figures, the blue lines indicate the lower limit of the entropy increase and the red line indicates the upper limit of the entropy increase.

There are other ways to measure the entropy of a biosystem using Fokker-Planck equation which is discussed in detail in [17]-[22]. In these articles, the entropy is calculated in detail of a complex non-equilibrium biosystem.

5. Conclusion

In this study we have made an attempt to understand model independent mutations of normal and failed types through basic thermodynamics. We have shown that the entropy change for a normal mutation is much less compared to the entropy change in a failed mutation. This study is a very general one and not specific to any particular type of mutation. However, the figures show that if we apply this study to any specific mutation, the entropies should lie within the range as shown in the plots or close to the range within reasonable uncertainties. Our future work is to study a specific type of mutation and see how the basics of statistical and thermodynamical physics explain the mutations from an entropy understanding.

Acknowledgements

The authors thank Paolo Grigolini, Randal Hallford, Yelena Nemchen and Garrett Baughman for useful discussions throughout the project.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Gerstung, M., Jolly, C., Leshchiner, I., Dentro, S.C., *et al.* (2020) The Evolutionary History of 2,658 Cancers. *Nature*, **578**, 122-128. https://doi.org/10.1038/s41586-019-1907-7

[2] Mutation, Learn Science at Scitable (2018) Nature Education.

[3] Sharma, S., Javadekar, S.M., Pandey, M., Srivastava, M., Kumari, R. and Raghavan, S.C. (2015) Homology and Enzymatic Requirements of Microhomology-Dependent Alternative End Joining. *Cell Death & Disease*, **6**, Article No. e1697. https://doi.org/10.1038/cddis.2015.58

[4] Chen, J., Miller, B.F. and Furano, A.V. (2014) Repair of Naturally Occurring Mismatches Can Induce Mutations in Flanking DNA. *eLife*, **3**, Article No. e02001. https://doi.org/10.7554/eLife.02001

[5] Bertram, J.S. (2000) The Molecular Biology of Cancer. *Molecular Aspects of Medicine*, **21**, 167-223. https://doi.org/10.1016/S0098-2997(00)00007-8

[6] Aminetzach, Y.T., Macpherson, J.M. and Petrov, D.A. (2005) Pesticide Resistance via Transposition-Mediated Adaptive Gene Truncation in Drosophila. *Science*, **309**, 764-767. https://doi.org/10.1126/science.1112699

[7] Burrus, V. and Waldor, M.K. (2004) Shaping Bacterial Genomes with Integrative and Conjugative Elements. *Research in Microbiology*, **155**, 376-386. https://doi.org/10.1016/j.resmic.2004.01.012

[8] Wallace, D.C. (2012) Mitochondria and Cancer. *Nature Reviews Cancer*, **12**, 685-698. https://doi.org/10.1038/nrc3365

[9] Weinberg, F., Hamanaka, R., Wheaton, W.W., Weinberg, S., Joseph, J., Lopez, M., *et al.* (2010) Mitochondrial Metabolism and ROS Generation Are Essential for Kras-Mediated Tumorigenicity. *Proceedings of the National Academy of Sciences of the United States of America*, **107**, 8788-8793. https://doi.org/10.1073/pnas.1003428107

[10] Petros, J.A., Baumann, A.K., Ruiz-Pesini, E., Amin, M.B., Sun, C.Q., Hall, J., *et al.* (2005) mtDNA Mutations Increase Tumorigenicity in Prostate Cancer. *Proceedings of the National Academy of Sciences of the United States of America*, **102**, 719-724. https://doi.org/10.1073/pnas.0408894102

[11] Mullen, A.R., Wheaton, W.W., Jin, E.S., Chen, P.H., Sullivan, L.B., Cheng, T., *et al.* (2011) Reductive Carboxylation Supports Growth in Tumour Cells with Defective Mitochondria. *Nature*, **481**, 385-388. https://doi.org/10.1038/nature10642

[12] Chure, G., Razo-Mejia, M., Belliveau, N.M., Einav, T., Kaczmarek, Z.A., Barnes, S.L., *et al.* (2019) Predictive Shifts in Free Energy Couple Mutations to Their Phenotypic Consequences. *Proceedings of the National Academy of Sciences of the United States of America*, **116**, 18275-18284. https://doi.org/10.1073/pnas.1907869116

[13] Daber, R. and Lewis, M. (2009) Towards Evolving a Better Repressor. *Protein Engineering, Design and Selection*, **22**, 673-683. https://doi.org/10.1093/protein/gzp051

[14] O'Gorman, R.B., Rosenberg, J.M., Kallai, O.B., Dickerson, R.E., Itakura, K., Riggs, A.D., *et al.* (1980) Equilibrium Binding of Inducer to Lac Repressor. Operator DNA Complex. *Journal of Biological Chemistry*, **255**, 10107-10114. https://doi.org/10.1016/S0021-9258(19)70434-7

[15] Raman, A.S., White, K.I. and Ranganathan, R. (2016) Origins of Allostery and Evolvability in Proteins: A Case Study. *Cell*, **166**, 468-480. https://doi.org/10.1016/j.cell.2016.05.047

[16] Ackers, G.K., Johnson, A.D. and Shea, M.A. (1982) Quantitative Model for Gene Regulation by Lambda Phage Repressor. *Proceedings of the National Academy of Sciences of the United States of America*, **79**, 1129-1133. https://doi.org/10.1073/pnas.79.4.1129

[17] Sharma, P. (2022) Fokker-Planck Equations, Entropy Production and Entropy Generation: A Review. *Research Trends and Challenges in Physical Science*, 7, 61-68. https://doi.org/10.9734/bpi/rtcps/v7/3346E

[18] Sharma, P. (2021) The Impact of Mutations: The Future of Cancer. *ScienceOpen Preprints*.

[19] Sharma, P., Hallford, R., Capotosto, S. and Smoot, B. (2020) Non-Equilibrium Entropy of Cancer Based on Gompertzian Growth. *Biophysical Journal*, **118**, 451A. https://doi.org/10.1016/j.bpj.2019.11.2514

[20] Capotosto, S., Smoot, B., Hallford, R. and Sharma, P. (2019) Entropy Production, Entropy Generation, and Fokker-Planck Equations for Cancer Cell Growth. *Physics*, **1**, 147-153. https://doi.org/10.3390/physics1010014

[21] Copling, S. and Sharma, P. (2018) The Impact of Mutations: The Future of Cancer. *Journal of Electrocardiology*, **51**, S83-S87.

[22] Houck, P.D. (2020) Making Drug Discovery More Efficient Applying Statistical Entropy to Biology. *Journal of Modern Physics*, **11**, 1969-1976. https://doi.org/10.4236/jmp.2020.1112124

Call for Papers

Open Journal of Biophysics

ISSN Print: 2164-5388 ISSN Online: 2164-5396
https://www.scirp.org/journal/ojbiphy

Open Journal of Biophysics (OJBIPHY) is an international journal dedicated to the latest advancement of biophysics. The goal of this journal is to provide a platform for scientists and academicians all over the world to promote, share, and discuss various new issues and developments in different areas of biophysics.

Subject Coverage

All manuscripts must be prepared in English, and are subject to a rigorous and fair peer-review process. Accepted papers will immediately appear online followed by printed hard copy. The journal publishes original papers including but not limited to the following fields:

- Bioelectromagnetics
- Bioenergetics
- Bioinformatics and Computational Biophysics
- Biological Imaging
- Biomedical Imaging and Bioengineering
- Biophysics of Disease
- Biophysics of Photosynthesis
- Cardiovascular Biophysics
- Cell Biophysics
- Medical Biophysics
- Membrane Biophysics
- Molecular Biophysics and Structural Biology
- Physical Methods
- Physiology and Biophysics of the Inner Ear
- Proteins and Nucleic Acids Biophysics
- Radiobiology
- Receptors and Ionic Channels Biophysics
- Sensory Biophysics and Neurophysiology
- Systems Biophysics
- Theoretical and Mathematical Biophysics

We are also interested in: 1) Short Reports—2-5 page papers where an author can either present an idea with theoretical background but has not yet completed the research needed for a complete paper or preliminary data; 2) Book Reviews—Comments and critiques.

Notes for Intending Authors

Submitted papers should not have been previously published nor be currently under consideration for publication elsewhere. Paper submission will be handled electronically through the website. All papers are refereed through a peer review process. For more details about the submissions, please access the website.

Website and E-Mail

https://www.scirp.org/journal/ojbiphy **E-mail: ojbiphy@scirp.org**

What is SCIRP?

Scientific Research Publishing (SCIRP) is one of the largest Open Access journal publishers. It is currently publishing more than 200 open access, online, peer-reviewed journals covering a wide range of academic disciplines. SCIRP serves the worldwide academic communities and contributes to the progress and application of science with its publication.

What is Open Access?

All original research papers published by SCIRP are made freely and permanently accessible online immediately upon publication. To be able to provide open access journals, SCIRP defrays operation costs from authors and subscription charges only for its printed version. Open access publishing allows an immediate, worldwide, barrier-free, open access to the full text of research papers, which is in the best interests of the scientific community.

- High visibility for maximum global exposure with open access publishing model
- Rigorous peer review of research papers
- Prompt faster publication with less cost
- Guaranteed targeted, multidisciplinary audience

Scientific Research Publishing

Website: https://www.scirp.org

Subscription: sub@scirp.org

Advertisement: service@scirp.org