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Human

# Should negative entropy be included in the fundamental laws of biology?

P D Houck[1,2*]

## Abstract

**Introduction**

Fundamental laws of biology are not currently recognized by biologists. Furthermore, negative entropy has been controversial since the concept was reshaped by the physicist Erwin Schrödinger. Self-organization, self-repair seems to be unique to biology; but, is clearly evident in the universe where galaxies sprang from hot plasma. Organization from chaos is possible if there are underlying fundamental laws that transforms chaos into organization. In biology, chaos within the DNA informational molecule results in mutations that allows life to survive when the environment changes. This is the underlying force of evolution. Disease is an expression of increased entropy and a new definition of disease is failure to maintain low entropy. Entropy is favorable promoting evolution so life can survive in a changing environment. Entropy is also unfavorable causing disease and individual lives to decay. Life has to combat entropy to maintain health.

Quantification of entropy by statistical mechanics can be accomplished by understanding life processes and probabilities at each stage of development and repair. These processes estimate of the inverse of disorder - organization. From these estimates the energy of syntropy can be estimated. Entropy is not time dependent but is process dependent since probabilities change at each stage of development. This method determines why men have shorter lives than women. The entropic power of the virome and microcosm are evident from their large numbers.

**Conclusion**

Entropy is critical to life, evolution, disease, health maintenance, biologic function, age, and eventual death. Life, as opposed to non-living, exhibits negative entropy; developing order out of chaos. (The energy to support negative entropy is yet to be defined.) This law indeed should be one of the fundamental laws of biology.

## Introduction

Fundamental laws of biology were proposed in an article in Heart Asia listed in table 1[1].

The laws of biology represent empirical observable facts. They are not accepted; since, unlike fundamental laws of physics, there have been no proposed laws of biology. These laws must be scrutinized by biologists before they are accepted. The topic of this paper is to address the most analytical law. Life, as opposed to non-living, exhibits negative entropy; developing order out of chaos. (The energy to support negative entropy is yet to be defined.)

Intuition into this law can be obtained through observation of the life cycle. At conception order is required for two cells to become one cell. On a molecular level maternal and paternal DNA has to unravel and recombine to form a unique set of instructions consisting of 46 chromosomes and an estimated 3.2 billion base pairs. The combination of base pairs encodes approximately 20 to 30,000 genes which produces proteins that give us our uniqueness. There may be as many as 2 million proteins with multiple folding configurations of side chains produced by the 20 to 30,000 genes. The proteins vary in size and are composed of 20 amino acids. These proteins generally determine the type and function of individual cells based on number of side chains and how the chains are folded. There are 50 to 100 trillion cells in an adult composed of 300 cell types. In each cell there are number of mitochondria that can reproduce on their own with its own set of DNA instructions to supply basic energy needs of cell. The processes of life must include the microcosm of bacteria that coexist in our body of another 500 to 1000 trillion bacteria with production of micro-RNA that co-ordinates bacterial function within the host milieu. The lowest order of inhabitants is the most numerous and consists of the virome which outnumbers the microcosom by 10 to 1 or greater.

## Discussion

**Developmental Biology**

As a baby grows into an adult and through middle age it harnesses energy from the environment and becomes more ordered. The zygote is a product of maternal and paternal DNA combining to have a full complement of genetic information. The entropy in this state is a reordering of base pairs. The cells in the blastomere then undergo mitosis and cleave multiple times without a change in total volume - approximately 16 cells. Despite appearing to be separate individual cells, the division is almost simultaneously accomplished. The DNA molecule is copied for each new cell. The spherical cell mass undergoes compaction to become the asymmetrical morula. Junctions appear for anchors and further growth results in an inside and outside arrangement. These cells from their programing develop the ability to shift fluid resulting in the separation of chambers by fluid. Further folding defines

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*Competing interests: None declared. Conflict of interests: None declared.*
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the origin of three major cell types, endoderm, mesoderm, and ectoderm. These layers will eventually further differentiate and become - digestive organs, lungs, kidneys, muscle, skeleton, blood, nervous system, skin, and hair. The order of development is very specific and is determined by genetic expression. The neural crest appears early in development and appears to have ordering and differentiating effect on structure. The different layers can combine so that elements from each layer may be represented in an individual organ. Blood vessels and nerves supply all of the organs forming a network of information and nutrient flow. This information is passed within protein receptors found on the cell surface that can communicate to the intracellular operation. In turn the machinery of the cells produces proteins that can be released into the surface of the cells or released into blood vessels to give information to other cells. Understanding this ordering in the day to day function of the cell is difficult. It is even more difficult to understand the energy required for a senescent cell to call for a replacement and recycle its cellular components performing self-repair. Self-repair begins to fail as we age, in part due to entropy. This is seen as degeneration of joints, hearing, vision, organ failure and eventual death[2].

**Biological Entropy**

In regard to entropy the temperature of the body is maintained in a narrow range around 37$^{o}$C so entropy is calculated at that temperature. In old age, tissues begin to lose order, replacement parts are not regenerated and degeneration ensues. Death is the maximum state of entropy when the body returns to ambient temperature.

Entropy Stress and Scaling of Vital Organs over Life Span by Kalyan Annamalai, and Carlos Silva proposes an interesting hypothesis that organ specific entropy determines life span[3]. This work is a follow up of Entropy Generation and Human Aging: Lifespan Entropy and Effect of Physical Activity Level by Carlos Silva and Kalyan Annamalai[4]. This result suggested reduced level of activity would prolong life. This statement is counter to most medical lifestyle recommendations. The organ specific paper is a refinement of the last paper sub-dividing total body entropy into organ entropy contributions. The result of this calculation appears to be in line with observed reasons for dying with cardiovascular disease as the number one cause. In both of these articles the authors use a classical thermodynamic definition for entropy to calculate life span - considering the human body to be similar to a combustion engine. This approach has merit.

Perhaps, a more appropriate analysis of entropy and Life would be to use a statistical mechanical definition. Life is self-reparative and self-organizing which sets it apart from the combustion engine. This concept intrigued the physicist Erwin Schrodinger who conceived of negative entropy to explain two cells becoming one with life having the property of self-organization deriving energy from the environment. Schrodinger's intuition into life processes is significant and he is credited with the concept of a molecule that would transfer information in biological systems. In 1944 DNA had not been elucidated and this concept was the corner stone that lead to its discovery [5].

It is best to use Schrödinger's own words to defend the concept of negative entropy.

"Erwin Schrödinger (1944), "What Is Life? : The Physical Aspect of the Living Cell". This excerpt is based on lectures delivered under the auspices of the Dublin Institute for Advanced Studies at Trinity College, Dublin, in February 1943.

Entropy = k log D, where k is the so-called Boltzmann constant = ( 3.2983 x $10^{24}$ cal./C), and D a quantitative measure of the atomistic disorder of the body in question.

**Organization maintained by extracting 'Order' from environment.**

How would we express in terms of the statistical theory the marvelous faculty of a living organism, by which it delays the decay into thermodynamical equilibrium (death)? We said before: 'It feeds upon negative entropy', attracting, as it were, a stream of negative entropy upon itself, to compensate the entropy increase it produces by living and thus to maintain itself on a stationary and fairly low entropy level. If D is a measure of disorder, its reciprocal, l/D, can be regarded as a direct measure of order. Since the logarithm of l/D is just minus the logarithm of D, we can write Boltzmann's equation thus:

-(entropy) = k log (l/D).

Hence the awkward expression 'negative entropy' can be he replaced by a better one: entropy, taken with the negative sign, is itself a measure of order. Thus the device by which an organism maintains itself stationary at a fairly high level of the orderliness (= fairly low level of entropy) really consists continually sucking orderliness from its

**Table 1: Laws of Biology.**

| | |
|---|---|
| 1 | Biology must be consistent with the fundamental laws of physics and chemistry. |
| 2 | **Life, as opposed to non-living, exhibits negative entropy; developing order out of chaos. (The energy to support negative entropy is yet to be defined.)** |
| 3 | The cell is the fundamental unit of biology |
| 4 | The cell must be in homeostasis with its environment. (This property allows forEvolution. The environment changes life.) |
| 5 | There must be a distinction between self and the environment. (Immunity andinflammation are the defenses against invaders from the environment *andresponsible for repair of damaged and senile cells*) |
| 6 | Electromagnetic information transfer is necessary for development andregeneration. (Life, regeneration of tissue will not exist in a non-electromagnetic environment, denervation)" |

*Competing interests: None declared. Conflict of interests: None declared.*
*All authors contributed to conception and design, manuscript preparation, read and approved the final manuscript.*
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environment. This conclusion is less paradoxical than it appears at first sight. Rather could it be blamed for triviality? Indeed, in the case of higher animals we know the kind of orderliness they feed upon well enough, viz. the extremely well-ordered state of matter in more or less complicated organic compounds, which serve them as foodstuffs. After utilizing it they return it in a very much degraded form –not entirely degraded, however, for plants can still make use of it. (These, of course, have their most power supply of 'negative entropy' the sunlight) "[6]

Indeed biological system may give insight to new laws of physics that could also explain the organization of the universe which appears to be also self-organizing. Regenerative ability and self-assembly of life should not be ignored in calculating the effect of entropy. This process has no rigorous mathematical approach. It perhaps can be framed by estimating the energy to build one cell. Empirically this could be determined by nutrient use of cell culture. One can then calculate energy required to lift the cell and assemble it into a 300 foot sequoia tree. By controlling the number of photons shinning on the tree one could see if there is an energy difference, i.e. negative entropy. Statistical mechanical entropy may be more appropriate for this analysis since every conceivable method of placing the cells would need to be considered.

Death seems easy to define and is thought to be when entropy is greatest with disarray of DNA, proteins, excessive fibrosis replacing regenerative cells. This natural form of death is determined by the organ most likely to fail as described by Annamalai and Silva. Most of the time death occurs prematurely as a result of an environmental stressor such as an infection or an injury from a fall. Death statistics are not very good at assigning a cause of death and frequently because the heart stops cardiovascular disease is labeled the cause. Dementia with failure to thrive can cause the heart to cease so vital statistics can be biased and may not be the best test of this theory. The organ system that is responsible for most deaths is not included in their analysis. This organ system is the endothelium which is the single layer of cells that lines all vessels - arteries, veins, capillaries, and lymph. By volume it is the largest organ. Endothelial dysfunction, wear of the blood vessels, failure to repair the lining of the blood vessels is what determines heart attack, stroke, and cancer development. The heart, brain, kidney and liver, all pay homage to the little endothelial cell; which determines vascular supply and a path for regenerative cells. Repair of the endothelium requires circulation of stem cells. Physical activity increases the circulation of these reparative cells and may explain how physical activity can be both detrimental in increasing entropy and beneficial in self-repair and decreasing entropy [7,8,9].

The brain should be reanalyzed since simple scaling of organ to mass may not apply to this solid organ. The scaling exponent is determined by circulation which is represented as a geometrical constant of mass to surface area. The brain is convoluted giving a much greater surface area to mass ratio. If this is taken into account, the final analysis will be the brain has the most heat generation as entropy and the most likely organ to fail if endothelium is ignored. Nutrient use is different for different organs with the brain preferring glucose. This fact may need to be modeled since different organ can utilize nutrients differently.

Organ recovery after cardiac arrest (a temporary death associated with maximal entropy), may be a better measurement tool than death statistics. The recovery of organs may in part be related to the individual organs ability to correct the increased entropy resulting from death. The brain is the least forgiving; the heart is much more forgiving. The kidney is more tenuous than the lung and the liver usually recovers in part due to its greater regenerative ability. Initiating hypothermia after cardiac arrest has been the most successful in preserving organ function and potentially provides a sink for release of built up entropy.

**Table 2: Statistical components of the body.**

| **Components of $D_{body}$** | |
|---|---|
| Chromosomes | 46/45 M/F |
| Base pairs in DNA | $3.2x10^9$ |
| Genes | $20x10^4$ to $30x10^4$ |
| Proteins | $2x10^6$ |
| Protein chains | n |
| Folding of Protein Chains | m |
| Amino Acids | 20 |
| Cell Types | 300 |
| Cells | $50x10^{12}$ to $100x10^{12}$ |
| $D_{mitochondria}$ | |
| $D_{microcosm}$ | |
| $D_{virome}$ | |

**Table 3: Statistical components of mitochondria.**

| **Components of $D_{mitochondria}$** | |
|---|---|
| Base pairs in DNA | $1.6x10^4$ |
| Genes | 37 |
| Proteins | 615 |
| Protein chains | n |
| Folding of Protein Chains | m |
| Amino Acids | 20 |
| #/Cells | $pX10^9$ mitochondria / ml cell type |

*Competing interests: None declared. Conflict of interests: None declared.*
*All authors contributed to conception and design, manuscript preparation, read and approved the final manuscript.*
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**Calculating the Energy of Biological Entropy**

The energy of the cell is provided by a miraculous structure. The mitochondrion is similar to ancient bacteria. This membranous cellular structure can reproduce by fission and can recombine with fusion. The greater number of mitochondria in the cell the more power can be delivered. Cells that require a lot of energy have many. Cells that are starved of mitochondria do not replicate themselves and cease the cell cycle. Just like bacterial cells there is information stored in mitochondrial DNA (mitochondrial genome). There are 37 genes made of 16,600 base pairs that encode 615 proteins. The Mitochondria in the female egg serve as the primary source of mitochondria in the offspring. The mitochondrial DNA can be used to trace female origin for many generations. These structures are self- organizing independent of the somatic cell DNA.

Law 2 was utilized in a paper, "Why is there a young woman advantage? Why is it lost? Applying the Laws of Biology to Men and Women" 7. The paper attempted to build on the statistical concepts of Erwin Schrödinger. A passage from this paper has been modified. "Entropy has been expressed in a classical form $\Delta S = dQrev/T$ and in a statistical form -(entropy) = k log (l/D) where k is the Boltzmann constant = 3.2983 x $10^{24}$ cal./$C^0$ and D is a statistical measure of disorder. Disorder can be calculated by all of the combinations of the elements of life. "

$D_{body}$ = chromosomes x base pairs in DNA x genes x proteins x protein chains x folding of protein chains x amino acids x cell types x cells x $D_{mitochondria}$ x $D_{microcosm}$ x $D_{virome}$

$D_{mitochondria}$ = base pairs in DNA x genes x protein x amino acids x number of mitochondria/cell ($D_{mitochondria\ Heart/ml}$) = 16,600 x 37 x 615 x 20 x 637X$10^9$mitochondria / ml Left heart

$D_{microcosm}$ = number of cells x number of cell types x chromosomes x base pairs in DNA x genes x proteins x protein chains x folding of protein chains x amino acids

$D_{virome}$=number viruses x number of virus types x number of base pairs in RNA/DNA components (positive +sense, negative – sense, ambisense.

Table 2, 3, 4 and 5 provide estimates of disorder of life components. The tables are incomplete and need expanded as our knowledge of biological processes increase. The tables also demonstrate the influence of the microcosm on entropy. The tables suggest the makeup of the bacterial flora, and the extensiveness of the virome contributes to entropy by their large numbers. Their contribution to increased entropy is a factor in longevity.

Order, however, can come from disorder with the help of the environment and natural selection. Entropy of all of the components of life shapes the evolution of life. The virome has the greatest entropy and its introduction into bacterial and mammalian cells is responsible for the mutations that have allowed the evolution of life. Entropy may contribute to our individual death, but assures preservation of life during environmental changes. The disorder of the virome introduced into the DNA can cause mutations that are

**Table 4: Statistical components of the microcosm.**

| Components of $D_{microcosm}$ | |
|---|---|
| # of cell | $500x10^{12}$ to $1000x10^{12}$ |
| # of cell Types | 10,000 |
| Chromosomes | 1 |
| Base pairs in DNA | $1.6x10^5$ to $1.3x10^7$ |
| Genes | 1000 |
| Proteins | ? 2 to 3,000,000 |
| Protein chains | n |
| Folding of Protein Chains | m |
| Amino Acids | 20 |

**Table 5: Statistical components of the virome.**

| Components of $D_{virome}$ | |
|---|---|
| # of viruses | $500x10^{13}$ to $1000x10^{13}$ |
| # of viral types Types | |
| Base pairs in RNA/DNA | 3,200 – $1.2x10^6$ |
| Genes | |
| +sense, -sense, ambisense | |
| Proteins | |
| Protein chains | n |
| Folding of Protein Chains | m |
| Amino Acids | 20 |

**Table 6: Calculations of various conditions of entropy.**

| condition | D | -(entropy) = k log 1/D |
|---|---|---|
| 2 cells becoming one cell | 2 | $-3.67x\ 10^{-23}$cal |
| 2 cells becoming a new set of DNA $3.2x10^9$base pairs selecting 2 at a time | $1.02e^{19}$ | $-2.31x10^{-21}$ cal |
| Protein production to allow cell division using 20,000 to 30,000 genes that form 2,000,000 proteins from 20 amino acids | | |
| Dividing 16 times to form Blastomere and reproducing mitochondria | | |
| Morula formation, junction, inside outside-endo meso epith layers | | |
| Further sequences in biologic process of development | | |
| Biologic sequence for cellular repair | | |
| Biologic sequence for defense from environmental hazzards | | |
| $10^{14}$ cells 300 at a time | | |
| | | Sum of Energies |

*Competing interests: None declared. Conflict of interests: None declared.*
*All authors contributed to conception and design, manuscript preparation, read and approved the final manuscript.*
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**Table 7: Disease and Entropy.**

| Disease/Affliction | Component of life | Defect Promoting increased entropy | Entropy Intervention |
|---|---|---|---|
| Age | Chromosomes | Failure to copy DNA correctly | Increase Telomere length |
| Age | Cells | Decreased stem cells | Increase stem cells |
| Age / red cell aplasia | Types of Cells | Lack of red cell precursor | Replace Red Cell Precursor |
| Age/ Hutchinson-Gilford's progeroid syndrome | Genes | mutation in LMNA | Replace Gene |
| Evolution | Base pairs | Point mutation | Depending on the environment this could be helpful or harmful in entropy |
| Alzheimer's Dementia | Protein Folding | Abnormally folded amyloid beta protein | Inhibit protein productionRefold miss-folded protein |
| Amyloidosis | Proteins, Protein Chains, Protein Folding | beta-pleated sheet conformation | Inhibit protein productionRefold miss-folded protein |
| Prion Disease "mad cow disease" | Protein Folding | Miss-folded protein of a normally produced protein | Inhibit protein productionRefold miss-folded protein |
| Sickle cell Anemia | Proteins, Protein Folding | Mutation Glu to Val distorts B- subunit | Replace Gene |
| Parkinson's Disease | Protein Folding | Non-functioning chaperone Protein | Infuse functioning chaperone protein |
| Anoxic Brain Injury | Cells | Apoptosis | Cooling protocols - a sink for excess entropy |
| Viral virulence | Protein Receptor | Mutation | Ig construction |

harmful or beneficial. The environment will select the favorable changes and those that are not will be lost. Chaos can beget order under the influence of negative entropy.

It is possible to calculate syntropy using Schrödinger's equation if disorder can be estimated. "For example, just considering 50 trillion cells of 300 cell types – There are approximately $5.6e^{4109}$ permutations for these two combinations of total cells and cell types. The energy for this state is $-5.11x10^{19}$cal. When considering all of the probable states, D is a very large number since every configuration of each subgroup and every configuration of subgroups is probable; therefore, as individuals, we are unique. In terms of numbers - There are 46 male chromosomes and 45 female chromosomes (one X is blocked), 3.2 billion base pairs, 20 to 30,000 genes, 2 million proteins, "n" number of chain configurations, "m" ways of folding, 20 amino acids, 50 – 100 trillion cells of 300 cell types, 500-1000 trillion cells of the microcosm, 5000-10,000 trillion virus. In terms of entropy - women have one less chromosome and therefore require less energy to maintain order. Law 2 suggests men will more quickly obtain the maximum entropy state – Death. Women will outlive men. Entropy would predict men will live shorter by an estimated (1-45/46) x 80 years = 76.5 years 3.5 years shorter over an average lifespan." [10]

Negative entropy can be calculated for living organism by number crunching all of the permutations listed for biologic processes. The order of calculating "D" needs to be in the specific order that reflects the development and growth of the organism, and later repair and maintenance. Biologic processes occur over time; however, the entropic energies are not time dependent. Entropic energies are dependent on the sequence of the biologic process. Entropy only considers the instantaneous probability states of order and disorder. The order of entropic forces is pre-specified in DNA. Each stage of development has specific entropy for that process. The process of cell union from one egg and millions of sperm, the unraveling and recombination of DNA, multiple protein production, production of cellular organelles, mitochondria, cell division, definition of architecture that directs embryonic development, and cell differentiation into cell types occurs in specific manner. Each step has an entropic energy that involves all of the statistical components of life at a specific stage in development. All of these energies can be added to determine the total entropy over a lifetime. Table 6 is an incomplete attempt at categorizing these energies. The author is unable to complete this computation for a lifetime of biological steps, but entropy can be evaluated for individual steps and disease states. Conception can be calculated by the energy required for sperm to swim to the egg and penetrate its membrane. Energy is supplied to the sperm by its carbohydrate rich media and millions of sperm swimming in the same direction. This energy is on the same order of magnitude required for the entropic calculation of two cells becoming one $-3.67x\ 10^{23}$ cal.

**Entropy as a Contributor to Disease and to Survival**

Recognizing entropic changes as a disease state in an organism is helpful in finding cures that restore a low entropic state from a higher diseased entropic state. Table 7 lists a few disease states, the component of life, the defect that caused the higher entropy and biologic methods that could be used to lower entropy, thus resolving the diseased

*Competing interests: None declared. Conflict of interests: None declared.*
*All authors contributed to conception and design, manuscript preparation, read and approved the final manuscript.*
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state. These processes could be targeted to increase lifespan by decreasing entropy.

Biological methods of lowering entropy, (syntropy) include telomere length to protect information propagation, reproduction of stem cells and differentiated progenitor cells, chaperone proteins to configure protein branch changes, electromagnet information by nerve impulses. Entropy is also fundamental for species evolutions [11,12,13]. Mutations that occur under the influence of positive entropy have an advantage by providing adaptations to new environments. When the environment changes the higher entropic state has an advantage for species survival. Interventions that provide energy to combat disease states from increased entropy include replacing stem cells, gene repair, increasing length of the telomere, refolding miss-shaped proteins or inhibiting their production.

**Corollaries from Biological Entropy Applied to Physics**

1. Entropy is not time dependent
2. Organization from chaos is possible through underlying fundamental laws that transform chaos into organization.
3. Decreasing entropy favors stability
4. Increasing entropy favors both destruction and creation

## *Conclusion*

Negative entropy as defined by Schrödinger can provide computational information of the processes of life – how it began, development of the organism, evolution, disease, and eventual decay into death. Disease has many definitions; a new definition of disease is failure to maintain low entropy. Entropy is critical to life, evolution, disease, health maintenance, biologic function, age, and eventual death. Life, as opposed to non-living, exhibits negative entropy; developing order out of chaos. (The energy to support negative entropy is yet to be defined.) This law indeed should be one of the fundamental laws of biology.

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*Competing interests: None declared. Conflict of interests: None declared.*
*All authors contributed to conception and design, manuscript preparation, read and approved the final manuscript.*
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