 doi:10.20944/preprints201909.0141.v1

Article

Shannon entropy of epithelium and five-fold morphology: A fundamental model to explain geometrical organizations as a source of information in biological systems

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Abstract: Based on a measuring system to determine levels of spatial organization in 2D polygons (homogeneous or heterogeneous partition of defined areas) lying on principles of regularity, we propose the entropy term linked to the concept of "information", from the "information theory field", in order to obtain an information measurement regarding a quantity of or amount of information in the architecture of complex 2D biological organizations. The term "quantity" does not refer to the amount of data (size), but to the probability of a geometrical basic pattern within a set of possible statistical configurations regarding levels of homogeneity and heterogeneity. It is this notion of information that is important in information theory, and measures of information in units of bits, what we propose to use for measuring quantities of organization in the architecture of complex geometrical systems. Two complex systems are tested, biological and non biological in order to obtain experimental results, which are verified with the evaluation criteria "entropy". Experimental results show that the lowest levels of information and entropy, in addition with low rates of heterogeneity and high rates of homogeneity are particular features of geometrical organizations in biological systems.

Keywords: biocomplexity; self-organization; spatial organization; geometrical shape; information theory; entropy.

1. Introduction

Informational entropy allows the quantification of order and disorder levels from discrete variables. The outline of an area or figure is a shape which can be a determined configuration of discrete elements or geometric parts. Accordingly, the focus of our view regards on basic principles of larger whole organization of polygons rather than just on properties of basic building blocks. In the context of shapes and forms in biology there have been an important historical effort in order to find the properties of patterns and the nature of those building blocks, looking at them from different levels, since a botton-up logic of biological developing structures, up to dynamical patterns, or even as whole organisms made of atomic parts (i. e., systematics). The boundless and overwhelming amount of configurations and patterns in complex living systems has been an elusive endeavor to understand, not just in terms of their categorization, but whether or not their

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geometrical principles are articulated as either a consequence or as an actual source of variability during evolution in the context of complex adaptative systems. There have been a great number of attempts during the history of biology to approach shapes and forms, with an equal width number of perspectives ranging from evolutionary and developmental biology to paleontology, theoretical morphology and taxonomy, just to include some examples. On the other hand, some non biological perspectives have been throughout that path of deep questions about shapes [1], and the logic of architecture order in nature [2]. In fact, all of those questions had endorsing important inferences to distant academic areas such as, material sciences [3], medicine [4, 5, 6, 7], even aesthetics, philosophy [1] and arts [9]. In addition, the mathematical perspective of topology, dynamical systems and other important areas related with geometry, statistics and discrete mathematics have been involved in a lot of important achievements [10, 11, 12, 13], mainly tracked by new emerging questions rather than achieving solid answers, all of this in the face of looking for particular levels of order in biological forms. In the context of the perspective of this paper, those properties of individual discrete elements in forms are not simple intrinsic features, instead, they must be understood as both, a space into a larger whole and as a unity defining that larger whole. In this line, our main question arose: There is a way to quantify geometrical order in a biological organization? In fact, in some sense it is not a novel question. There have been an important amount of works related with the issue of quantifying information at different complexity levels in biological networks [14, 15, 16, 17], ecosystems [18, 19, 20, 21, 22], molecular entropy [23], cell entropy [24, 25], just to mention some. Also, forms of spatial entropy looking for the characterizing of landscape heterogeneity, urban, sociological and economical properties associated to them have been broadly approached [26, 27 & 28]. However, in the context of biology the underlying order behind the geometry of general biological organizations is still lacking. We consider that the main obstacle in that general research direction is the establishment of a biological form of reference to start to work on.

The establishment of a measure of spatial organization able to determine the geometrical entropy of a particular biological organization was motivated and is derived from a previous analysis of geometrical constrictions in five-fold morphologies (polygonal random disc organizations [29]). Also, a lot of work has been done relating the larger geometrical context of cells, their entropy and the physical causalities of interactions into cell aggregates [30, 31, 32, 33, 34, 35 & 36]. However, all of this work is regarding on physical parameters and not strictly on levels of geometric organization. In addition, the characterization of self-assembled 2D Patterns with Voronoi Entropy in [37 & 38] also represents some sort of approaches about levels of generic heterogeneity at different scales achieving geometry as a source of organization. In spite of that, the main results of that kind of works release some ideas about entropy in a context of matter organization and ecological dynamics motivating some researches of material sciences and territory aspects, without go deep in questionings about the nature of order in biological shapes.

On this research work, we seek to establish a novel connection, between information theory [39] and the architecture of biological organizations. Since it is considered that, the statistical recurrence of geometric patterns in certain complex architectures, seen from its resulting distribution, codifies the key properties that emerge from the complex system, such as information (disorganization) and not information (self-organization). It is certainly not logical, but on the contrary, it is contradictory to associate self-organization with reductions in the entropy of systems. However, in previous investigations, such behavior has been associated [40, 41 & 43], and in this work we will try to verify it. If there is more self-organization in a system, then its behavior will be less entropic, and therefore the information in it will be smaller, which is contradictory, since it would be thought of naturally that, being more self-organized, it is feasible to extract more information from such a system.

Due to the above, in this work we propose to measure the quantity of information in geometrical patterns in the architecture of complex systems (biological and non biological polygonal arrangements), regarding the disorganization and self-organization metric based on their geometrical configuration.

To develop the idea, this paper is organized as follow: the mathematical model and the main background to define regularity and heterogeneity in spatial organization of shapes are given in

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Section 2.1 and 2.2. in methods. The structure of the proposed method, to determine the entropy of discrete variables and statistical distributions of internal partitioning in shapes Γ and the procedure to measure the quantity of information in geometrical patterns in the architecture of biological and non biological systems, is presented in Section 2.3 and 2.4. Results and analysis in terms of entropy are provided in Section 3 and finally in Section 4 the discussion and conclusions are presented.

2. Methods

2.1. Regularity and heterogeneity in spatial organization of shapes Γ.

The establishment of a measure of spatial organization able to determine the geometrical entropy of biological organizations is derived from a previous analysis of geometrical constrictions in five-fold morphologies [29]. In this new work our main methodology is centered on statistical measurements of geometrical heterogeneity and their related entropy. The aim of our methodology regards for determining levels of homogeneity-heterogeneity and levels of information associated to biological organizations. The statistical analysis is derived from the study of localities and their sub-localities arising from constructions generically named shapes Γ. A shape Γ is a set of spatial planar confined regions called sub-localities inside a locality L_i. Therefore, a shape Γ could be a regular or irregular polygon. On that sense, each shape Γ has an area distributed inside L_i that can be subject to be statistically analyzed. The main idea to establish the generic name of shape Γ is due to it is useful to define either polygons or areas (numeric values) associated with particular shapes.

Each locality L_i is constituted by a subset of a given number N_i of sub-localities, $S_{i1}, S_{i2}, \dots, S_{iNi}$ such that $L_i = \cup_{j=1}^{N_i} S_{ij}$, where L_i is a spatial region which could be a convex polygon in $\mathbb{R}^2$. Let A_{ij} be the area of each sub-locality. If $A_{ij} = A_{ik} \forall\, k, j$, then we said that L_i is regular (Figure 1). In contrast, if exists some $j \neq k$ such that $A_{ij} \neq A_{ik}$ then we say that L_i is not regular and it can be considered either a highly homogeneous or a heterogeneous partition. Therefore, let $A_i = \sum_{j=1}^{N_i} A_{ij}$ be the sum of all the associated areas of every locality; this set determines a polygon or shape $\Gamma = \{A_i\}$. Therefore, Γ is a generalization of locality or any set of sub-localities which are considered in numerical terms. Therefore, the area average of a locality L_i is:

$$\bar{A}_i = \frac{1}{N_i} \sum_{j=1}^{N_i} A_{ij} \tag{1}$$

and

$$\sigma_i = \sqrt{\frac{1}{N_i - 1} \sum_{j=1}^{N_i} (A_{ij} - \bar{A}_\iota)^2} \tag{2}$$

is the standard deviation of each locality. Notice that if $\sigma_i = 0 \Rightarrow A_{ij} = A_{ik}\ \forall\, j, k$; therefore that locality is regular.

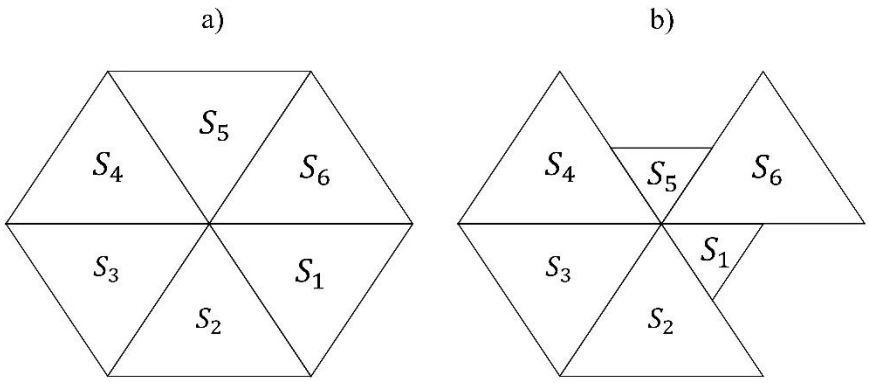

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Figure 1. Schematic properties of two different shapes Γ. a) An hexagon is a locality associated to six subareas from four sub-localities $S_1, S_2, \ldots, S_6$ which are all equal then is regular. b) A shape Γ with a six-fold partition such that any of their sub-localities have unequal subareas is not regular; the set of areas defined by sub-localities $S_1$and S_5 are smaller than S_2, S_3, S_4 and S_6.

2.2. Standard deviations of five-fold symmetry as a reference of highly homogeneous partitions for biological organizations.

The main objective of our research is the establishment of a measure of spatial organization able to determine the geometrical entropy of biological organizations regarding particular geometries as references. In a previous paper we have shown homogeneity variations in a set of polygonal discoid arrangements with partitions of several numbers. We relate equation (2) with a proper collection of data reflecting rates of spatial heterogeneity, quantifying indexes of standard deviations of areas in all of our theoretical samples. Our geometrical design has as a first condition the fact that, planar discs with different number of sub-localities remains with an almost constant area during the experiment in order to have normalized data [29]. Although we consider partitions of discs ranging from three to ten sob-localities and each partition with a constant area during the experiment, we include ten levels of variability (Figure 2). That variability certifies that our model includes a broad range of random partitions inside discs controlling the polygonal number of sides in a well confined space. For this purpose, we use Voronoi diagrams to model space partitioning with different number of parts (from three to ten), where two variables were studied, namely, partitioning number and partition variability. The algorithm to build partitioning and levels of variability of discs is described in detail in reference [29]. Our final conclusion in that work was that highly homogeneous partition of internal space can be considered as a geometrical constraint in five-fold symmetry against any other (Figure 3), and this kind of highly ordered partition can be considered as a functional geometrical particular feature of biological organizations. Since five-folding often is an arrangement associated with biological architectures, we consider this organization and their features as a first clue. In addition, it is an intuitive fact that four and six folding partitions are also frequent architectures in nature (e. g. flowers). To continue with this hypothesis we need to develop a formal procedure to understand differences between biological and non biological organizations in terms of information using entropy equations.

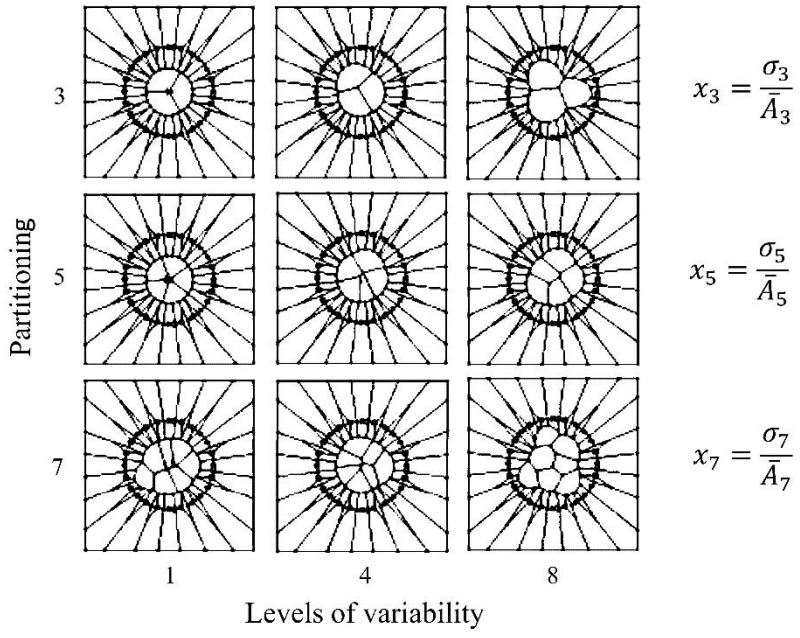

Figure 2. The source of variability. Random discs are build up to generate statistical data of shapes Γ. The generic expression $x_i = \sigma_i/\bar{A}_i$ is shown using three examples in order to determine

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heterogeneity using different levels of variability (horizontal axis) and different partitions of discs (vertical axis).

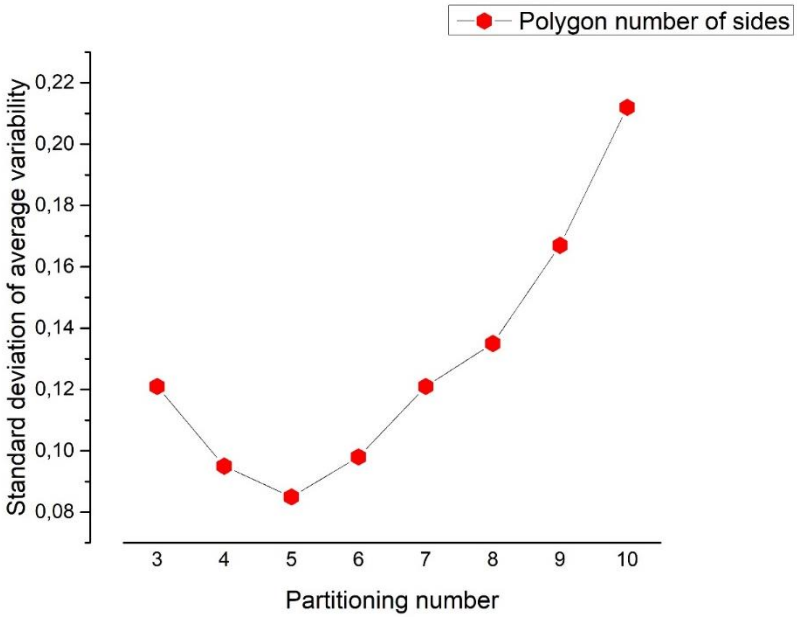

Figure 3. Standard deviation of all variability averages for each partitioning number. An average of standard deviations ($\bar{\sigma}_i$; variability average) was derived for each level of variability. A standard deviation of all variability averages is obtained for each partitioning number. According to this data, five-fold organizations are at the lowest level of dissimilarity among areas inside discs.

2.3. Entropy of discrete variables and statistical distributions of internal partitioning in shapes Γ.

The Shannon entropy is a parameter indicating information which is a resolution of uncertainty. Our model satisfies the fact that we may work with frequencies of discrete variables which are areas of polygonal shapes. Shannon elucidates the convenience of the use of a logarithmic function in the definition of the entropies, what it is mainly because mathematically "it is more suitable", because many limiting operations in terms of the logarithm are simpler than in terms of the statistical behavior (the number of possibilities or frequency).

One important and non trivial fact regarding polygonal geometry is the statistical behavior of inner area distributions in shapes $\boldsymbol{\Gamma}$. The heterogeneity of area distributions according to partitioning number reveals that the number of elements in a disc determines the homogeneity distribution of areas. In that sense, the frequency of distribution of heterogeneities is different in line with the geometrical nature of polygons. Thus, this difference might generate a parametric measure of either organization of internal spatial elements (sub-localities) or entropy. In line, the choice of a logarithmic base regards towards an election of a proper unit for measuring information. If the base 2 is used, the resulting unit is called 'bit' (a contraction of binary unit).

In consonance with this we consider frequency values of heterogeneity as discrete variables. The entropy of discrete variables could be defined as follows. The outcomes for heterogeneity levels can be tagged as a binary result:

$$X = \begin{cases} 0, & if\ the\ outcome\ is\ less\ than\ 0.5\ of\ heterogeneity\ x_{ih} \\ 1, & if\ the\ outcome\ is\ more\ than\ 0.5\ of\ heterogeneity\ x_{it} \end{cases}$$

With these definitions, one bit is the amount of information obtained when one of two equally likely alternatives is specified. Using this as reference the equation will define the entropy in terms of the frequency of two digits, 0 and 1. Therefore, we can use a well known entropy equation typically used to determine the uncertainty of outcomes:

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$$H_\Gamma(X) = p(x_{ih})log_2\left(\frac{1}{p(x_{ih})}\right) + p(x_{it})log_2\left(\frac{1}{p(x_{it})}\right) \quad (3)$$

where the next equation reflects the amount of heterogeneity,

$$x_i = \sigma_i/\bar{A}_i \quad (4)$$

we include $\bar{A}_i$ in order to normalize the data and constraint the heterogeneity outcomes inside a scale from 0 to 1.

2.4. Entropy in mosaics of cells.

Defining entropy in mosaics of cells requires the coordinates of individual polygons. Consequently, polygons were treated with a similar procedure applied to shapes Γ. Nonetheless, in this case there will not be a Voronoi treatment for points since each polygon has its own precise set of coordinates, generating N localities L_i (polygons), constituted by a subset of a given number N_i of sub-localities (triangles) per number of sides $S_{i1}, S_{i2}, \ldots, S_{i_{Ni}}$ defining standard deviation of internal areas (equation 4), where L_i is a convex regular or irregular polygon in $\mathbb{R}^2$ (Figure 4). In fact, we used random arrangements, and processed and non processed images extracted from different web sites and references [34, 42 & 43] to define the coordinates of polygons using the centroid of the polygon as the origin of polygonal coordinates. Therefore, three types of mosaics were analyzed: Random arrangements (RA), non processed images extracted from the web (epithelia and peripodial wing of imaginal disc; BIO) and processed images extracted from the web which we named control simulation (CS), simulation at equilibrium (SAE), atrophy simulation (AS), simulation out of equilibrium (SOE) and Poisson-Voronoi tessellation (PT). Spatial heterogeneity in mosaics of polygons was derived using equation (4) for each polygon and entropy using equation (3).

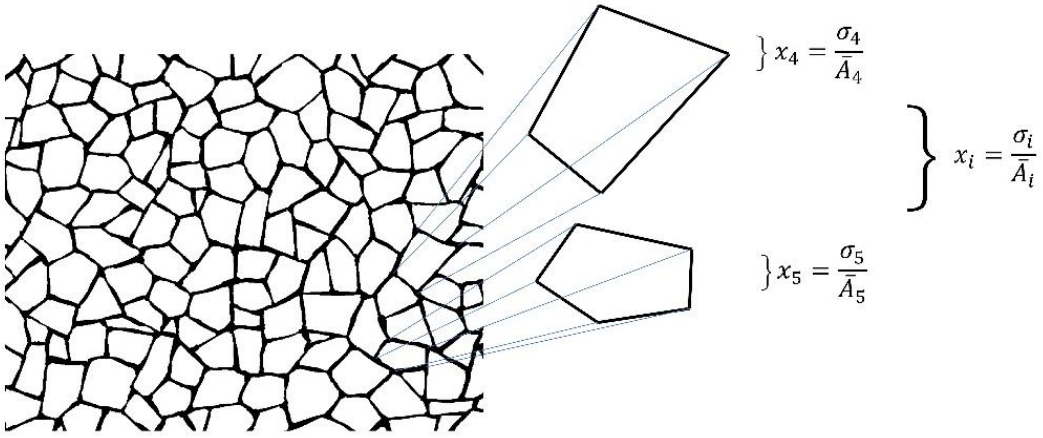

Figure 4. Symbology of equations for individual polygons extracted from a mosaics of polygons.

3. Results

According to partitioning number the heterogeneity distributions of shapes Γ is showed in figure 5. The bar area determines levels of heterogeneity conforming to the binary categorization 0 and 1 described before. The grey area shows levels of heterogeneity below 0.5 of SD indexes which implies either high levels of homogeneity or low levels of heterogeneity. It is clear that five-folding organizations have the lowest values for heterogeneity (green area) indexes indicating highest levels of homogeneity (grey area). In fact, this figure reflects the performance of spatial organizations that have been shown in figure 3. Regarding to this last point, it is important to focus on the fact that now we have these two necessary outcomes for heterogeneity which are used to define the entropy of internal partitioning in shapes Γ using equation (3).

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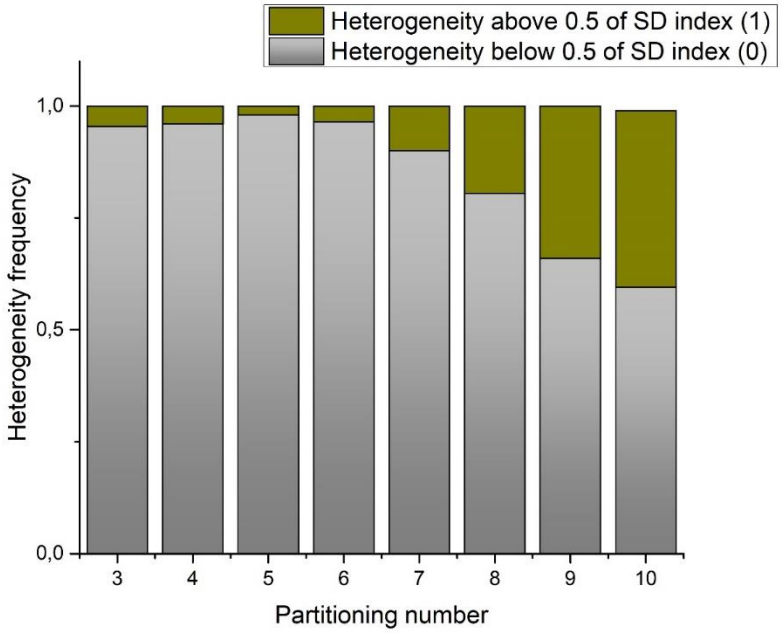

Figure 5. Levels of heterogeneity according to the binary categorization 0 and 1. Grey zones are values associated to 0 and the green ones are associated with 1. The highest level of homogeneity is for partitioning number five. The highest level for heterogeneity is for partitioning number ten.

In order to link entropy and information, our evidence suggests that five-folding organization depicts a sort of spatial organization with low values of information (Figure 6). In addition, the entropy values for spatial organizations also reflect being in line with figures 3 and 5. Hence, we consider this entropy measure as a solid argument to be applied not just on individual polygons, as we have done up to now, but to explore whether or not there are entropy differences between more complex biological and non biological organizations in terms of entropy.

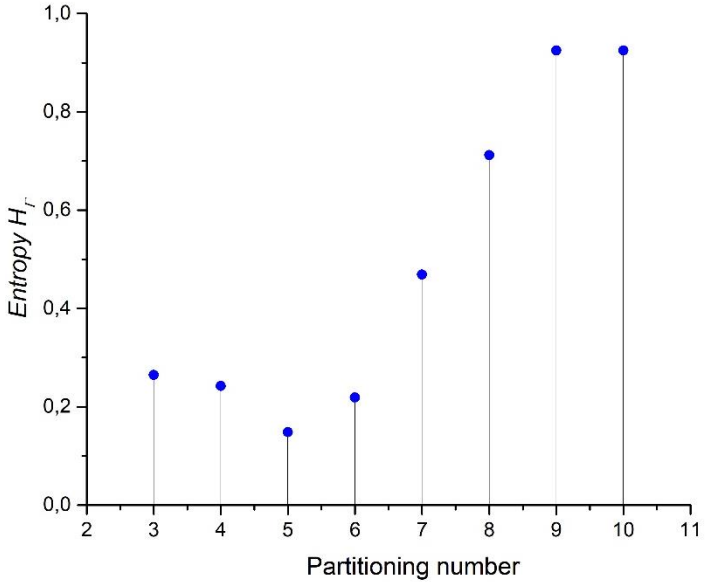

Figure 6. The entropy of shapes gamma H_Γ indicates that partitioning number five has the lowest value of entropy. Similar values are founded in 3, 4 and 6 organizations. The highest values of entropy are founded in 9 and 10 disc organizations.

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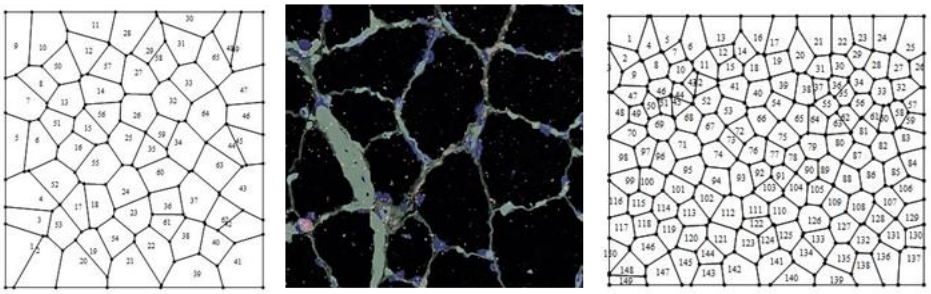

Figure 7. Three general types of mosaics analyzed. Left side; random arrangements (RA), center; non processed images extracted from the web (BIO) and right; processed images extracted from the web which we named they control simulation (CS), simulation at equilibrium (SAE), atrophy simulation (AS), simulation out of equilibrium (SOE) and Poisson-Voronoi tessellation (PT).

Spatial heterogeneity in mosaics of polygons was derived using equation (4) for each polygon. Interestingly, RA has an average of a half proportion of heterogeneity of spatial distribution on internal areas in polygons and a half of spatial homogeneity (Figure 8). Biological organizations of cells aggregates have a constant high proportion of homogeneity in terms of spatial distribution and BIO images were derived directly from images of biological organizations (Figure 9). CS, SAE, AS and SOE were computational simulations of cells aggregates assuming Lewis's Law or another kind of biological properties. In spite of that, our results shown that these images should also be considered as non biological samples since the entropy results depicts distant values of information except for AS and SAE (Figure 10 and 11). Poisson-Voronoi tessellation (PT) was used as control. Hence, the geometry between biological and non biological arrangements of internal cells is underlying an important difference whose consequences and effects would define particular behavior in biological organizations in contrast with non biological package.

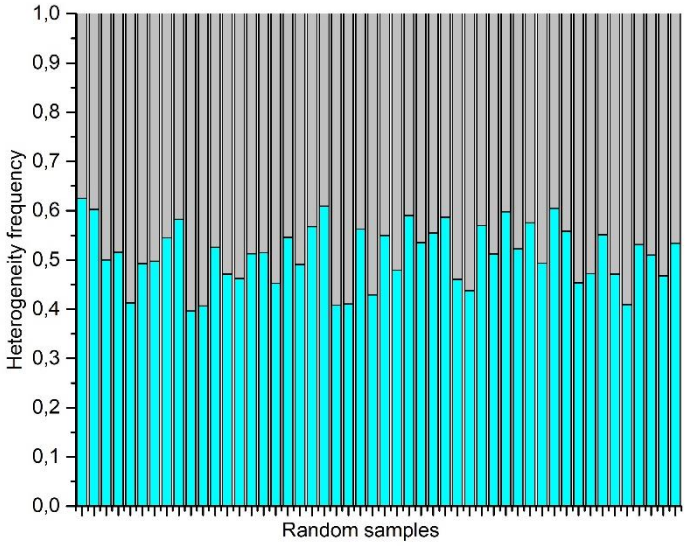

Figure 8. Random arrangements of cells and their heterogeneity frequency. Data shows that cellular aggregates have an average of a half proportion of heterogeneity (grey) of spatial distribution on internal areas in polygons, and a half of spatial homogeneity (blue).

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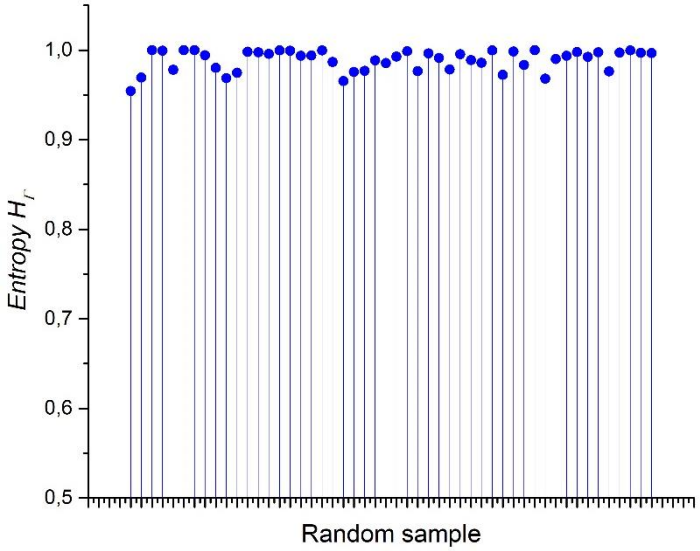

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266 **Figure 9.** The entropy of random samples. The entropy values are almost constantly in line with
267 maximum entropy.

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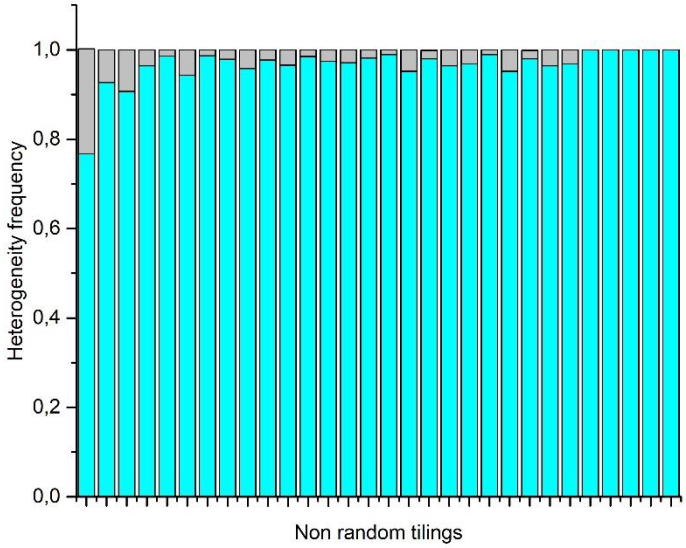

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270 **Figure 10.** Biological and biological simulations of organizations of cells aggregates have a constant
271 high proportion of homogeneity in terms of spatial distribution of inner areas. In fact, the last five
272 samples area biological simulations assuming Lewis´s Law with a 100% degree of homogeneity. The
273 first column represents a Poisson-Voronoi Tesselation was used as a control.

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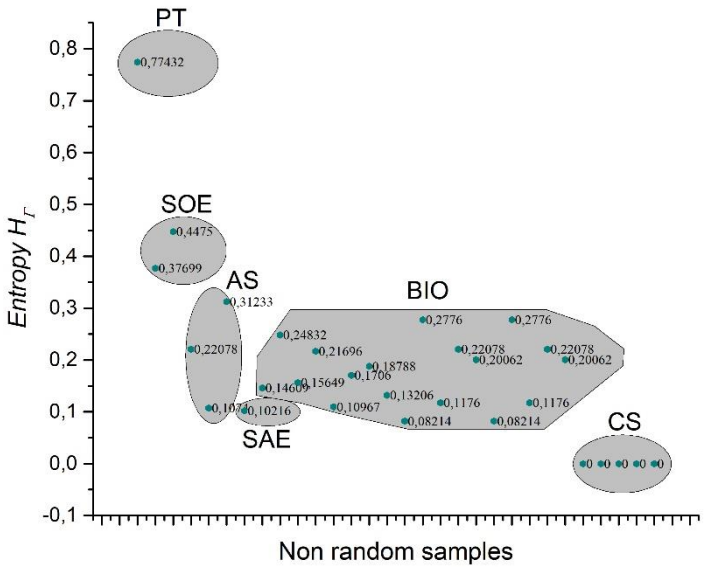

Figure 11. The entropy of cell aggregates groups: biological extracted images directly from the web (epithelia and peripodial wing of imaginal discs, BIO) and processed images extracted from the web which we named control simulation (CS), simulation at equilibrium (SAE), atrophy simulation (AS), simulation out of equilibrium (SOE) and Poisson-Voronoi tessellation (PT). The most abundant area includes Bio data and it also can include SAE and AS.

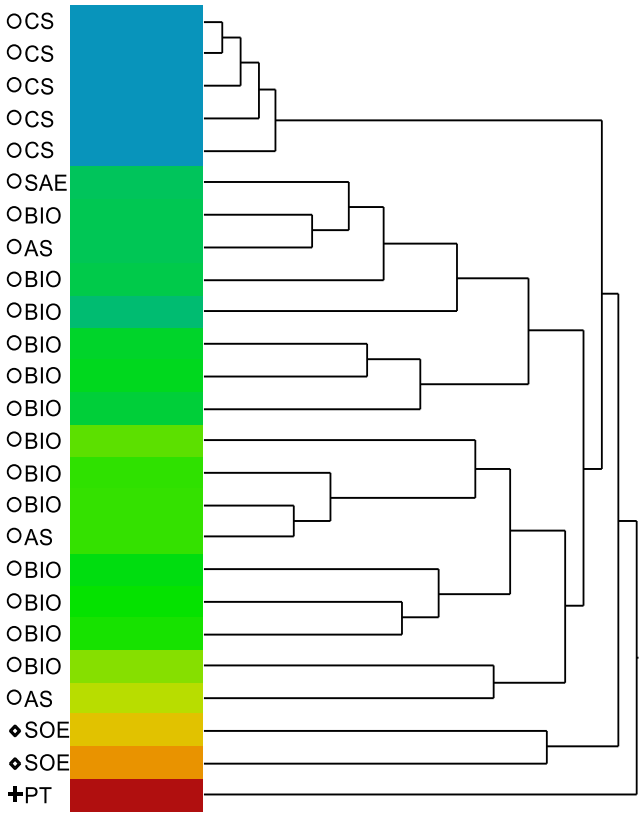

Figure 12. The Hierarchical clustering group entropy values which are close to each other relative to those of other clusters. Hierarchical clustering is a process that starts with each point in its own cluster. At each step, the two values that are closest together are combined into a single cluster. This process continues until there is only one cluster containing all the points. CS group entropy values of 0 and PT groups the highest value of entropy as control. Green values reflect clustering of BIO groups or closes groups. This analysis was done using JMP 8.

4. Discussion

The highest level of homogeneity for partitioning number five represents the establishment of a biological form of reference to start to work on. According to our binary partition of frequency distribution where below of 0.5 of heterogeneity represents 0 and above of 0.5 of heterogeneity represents 1, it is clear that five-folding arrangements distributes space in a very equal statistical possibility. Even there is an evident closeness with four and six folding partition there are statistical differences between them that were clear in a previous paper [29]. In terms of entropy derived from equation 3 five-folding partition reach the lowest point with a value of 0.14 (Figure 6). This finding is a non trivial fact, since we should not expect statistical differences between partitions if the source of variation is a random source and variability is included in all analyzed samples. We should expect no difference at all since it is a random experiment just varying partitioning. Hence, that gap of entropy values coming from four, five and six folding arrangements represents our main biological parameter of reference to start to work on with shape informational entropy (i. e. around 0.14 and 0.25 of entropy). Three types of mosaics were analyzed: Random arrangements (RA), non processed images extracted from the web (epithelia and peripodial wing of imaginal disc; BIO) and processed images also extracted from the web which we named control simulation (CS), simulation at equilibrium (SAE), atrophy simulation (AS), simulation out of equilibrium (SOE) and Poisson-Voronoi tessellation (PT) [images extracted from references 34, 43 & 44]. Spatial heterogeneity in mosaics of polygons was derived using equation (4) for each polygon and entropy using equation (3). Random arrangements of cells and their heterogeneity frequency shows that random polygonal aggregates representing cell aggregates have an average of a half proportion of heterogeneity of spatial distribution on internal areas in polygons with a nearby equal half of spatial homogeneity. Biological and biological simulations (which we has referred as non biological samples) of organizations of cells aggregates have a constant high proportion of homogeneity in terms of spatial distribution of inner areas. In fact, the last five samples area biological simulations assuming Lewis´s Law with a 100% degree of homogeneity. Then, a high degree of homogeneity in a computational simulation following some algorithmic instructions could derive in a beautiful representation of a biological sample, lacking of substantive information or levels of intrinsic disorder emerging from the actual biological form. On the other hand, BIO group is around 0.08 and 0.27 which are entropy values not so far from 0.14 and 0.25 for four, five and six folding partitions. Also, in figure 9 and 10 the first column represents a Poisson-Voronoi Tesselation which was used as a control. Even this sort of organization is not biological at all it seems far from random organizations. The most abundant area in figure 10 includes Bio data and it also could include SAE and AS. Simulation at equilibrium and atrophy simulation which are two kind of samples based on manipulated computational simulations. The closeness of them with BIO group is not an unexpected result since computational simulations representing algorithmic instructions are perturbed in a way that could easily increase their entropy. It does not happen with control simulations. Those algorithmic constructions are following mathematical prescriptions whose level of correctness leaves out the essential nature of BIO group which is a lightly bias disruption of order. In fact, control simulation group has a value of zero of entropy (Figure 10).

5. Conclusions

Our results reflect that there is an informational limit for biological organizations. According to this conclusion, biological organizations are complex systems which should be constrained into a narrow window of variability depending on levels of informational entropy. However, the fact is that we can see a myriad of morphological variations in nature. We conclude that the statistical properties of biological architectures can be manifested in an overwhelming amount of morphologies since all of them are singular possibilities in the realm of pure organization. In that sense, shape is a constant configuration changing of dynamical arrangements opening infinite possibilities of configurations with biological attributes as a consequence of its essential organization which depends on their own limits. According to our results, we consider that homogeneity with low levels of heterogeneity is a constant issue from many perspectives. Networks theory call it

sparcity, chaos theory refers to it in an interval between order and chaos. With this in mind, we consider that the value and limits of informational entropy for geometrical systems that we are approaching has a width domain of impact.

Author Contributions: For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used "Conceptualization, Juan López-Sauceda and José Gerardo Carrillo González; Methodology, Juan López-Sauceda, José Gerardo Carrillo González, Carlos Ortega Laurel, María del Carmen Mejía-Vázquez and Philipp von Bülow; Software, Juan López-Sauceda, José Gerardo Carrillo González and Philipp von Bülow; Validation, Juan López-Sauceda, José Gerardo Carrillo González, Carlos Ortega Laurel, María del Carmen Mejía-Vázquez and Philipp von Bülow; Formal Analysis, Juan López-Sauceda, José Gerardo Carrillo González, Carlos Ortega Laurel, Philipp von Bülow; Investigation, Juan López-Sauceda.; Resources, Juan López-Sauceda and José Gerardo Carrillo González; Data Curation, Juan López-Sauceda, José Gerardo Carrillo González and Philipp von Bülow; Writing-Original Draft Preparation, Juan López-Sauceda; Writing-Review & Editing, Juan López-Sauceda, José Gerardo Carrillo González, Carlos Ortega Laurel, Philipp von Bülow; Visualization, Juan López-Sauceda, José Gerardo Carrillo González; Supervision, Juan López-Sauceda; Project Administration, Juan López-Sauceda; Funding Acquisition, Juan López-Sauceda".

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

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