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A non extensive approach for DNA breaking by ionizing radiation.

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Abstract

Tsallis entropy and a maximum entropy principle allows to reproduce experimental data of DNA double strand breaking by electron and neutron radiation. Analytic results for the probability of finding a DNA segment of length l are obtained reproducing quite well the fragment distribution function experimentally obtained.

Atomic force microscopy (AFM) has revealed itself as an extremely useful device in the analysis of very small structures and specially in DNA fragment analysis as it has been shown in.[1]

It is interesting to study the production of fragments in DNA as a result of radiation, since the presence of radiation interacting with DNA molecules can influence the properties of living cells up to a lethal extreme.

On the other hand, DNA fragment analysis may help in the study of the structural properties of genome texts, and then to understand general principles of genetic sequences.

The process of DNA double strand breaking was performed by irradiation of DNA molecules with electrons and neutrons at different doses (See[1]). Then, the length of the resulting fragments was measured. As a result, the collection of fragments was found to obey a fragment size distribution function (FSDF), which presents important characteristics from the viewpoint of complexity.

The main fact, which will be focused in this paper, is that the collection of fragments is such that there is not a "characteristic" size of the fragments, *i.e.*, the smaller the fragment, the more abundant is it. The FSDF in this case does not present a definite local maximum, resembling more to an inverse power law, i.e., a distribution function in the basin of attraction of a stable (Lévy) distribution.[2]

The main distinction of Lévy distributions lies in the fact that their variance is divergent. Maybe because of it, scientists have paid attention to them only recently.

This feature of the FSDF is not new. It has been reported in[3] the occurrence of transition to scaling in FSDF during glass rods breaking, in[4] the power law distribution of fragments was related to self-organized criticality (SOC). Matsushita[5] proposed a fractal representation for a general process of fragmentation.

Our group[6,7] detected power law behavior in the process of liquid drop fragmentation and we proposed a Bethe lattice representation to interpret FSDF in these experiments.

Some attempts to relate FSDF to first principles in physics like the maximum entropy principle are present in[8,9] with results that, at the best, do not cover the process in which scaling in FSDF is present. (*i.e.*, when the energy of the fragmentation process is high).

The universal nature and almost unlimited range of applicability of the

maximum entropy principle leads us to expect it to be useful in describing scaling in FSDF even at DNA scale.

But the process of fractionating, by its own nature, is a paradigm of phenomena in which interactions are long-range correlated among all parts of the object under fragmentation. Then, though the maximum entropy principle is expected to have an unlimited range of application, in the process of breaking the expression for the entropy in its Shannon form:

$$S = -k \int p(x) \log p(x) dx \tag{1}$$

-where $p(x)dx$is the probability of finding the system magnitude x in the interval $[x, x + dx]$, and k is Boltzmann's constant- is not applicable.

This is because this formula, based in Boltzmann-Gibbs statistics, is expected to be valid when the effective microscopic interactions are short-ranged, and this gives to this entropy its extensive character (The entropy of the whole object equals the sum of the entropies of its constituent independent parts).

Since, as we already pointed out, all parts of the fractionating object during the process of violent breakage are correlated, then the entropy of the object being fractionated is smaller tan the sum of the entropies of the parts in which the object divides, defining this way a "superextensivity" in this system. This suggests that it may be necessary to use non-extensive statistics, instead of the Boltzmann-Gibbs one.

This kind of theory has already been proposed by Tsallis,[10] who postulated a generalized form of entropy, given by

$$S_q = k \frac{1 - \int p^q(x) dx}{q - 1} \tag{2}$$

where q is a real number.

This entropy can also be expressed as:

$$S_q = -k \int p(x) l_q p(x) \tag{3}$$

where the generalized logarithm $l_q p(x)$ is defined as (See[11]):

$$l_q(p) = \frac{p^{1-q} - 1}{1 - q} \tag{4}$$

It is straightforward to see that $S_q \longrightarrow S$ when $q \longrightarrow 1$, recovering Boltzmann-Gibbs statistics.

It is our goal to derive, starting from first principles, a functional dependence to describe the DNA DSDF obtained in.[1]

Starting from equation 2 we may follow the method of Lagrange multipliers to apply the maximum entropy principle to the fragmentation of DNA. To do this, we impose two constraints: The first is the trivial one of normalization of the probability:

$$\int p(l)dl = 1 \tag{5}$$

i.e., the sum of the probabilities of finding a fragment of any length is equal to unity.

As a second constraint we may choose to adopt a "q-mean value" as:

$$\int p^q(l)ldl = 1 \tag{6}$$

Which reduces to the classical mean value when $q \longrightarrow 1$ .In this formulation the length l of the fragments has been referred to a unit adequately chosen as to choose the "q-mean value" equal to one.

It may seem strange to introduce a "q-mean value" , also known as "unnormalized mean value" in this formulation. Really, this choice is not unique but for our purposes and for simplicity reasons we will choose this formulation. In[11] a detailed discussion of the possible choices for the second constraint can be found. The one here chosen showed to be particularly useful in describing anomalous diffusion and was also employed by us in[12,13] dealing with problems of fragmentation.

Now we use the method of Lagrange multipliers by means of the construction of the functional:

$$\pounds(p_i, \alpha, \beta) = S_q - \alpha \int p(l)dl + \beta \int p^q(l)ldl \tag{7}$$

being α and β the Lagrange multipliers.

The extremization of this functional leads to:

$$p(l_i) = \frac{\beta(2-q)dl}{[1+\beta(q-1)l]^{1/(q-1)}}; \tag{8}$$

Alternatively, the same method when applied to the Boltzmann entropy ($q = 1$) gives

$$p(l)dl = \beta e^{-\beta l} dl. \tag{9}$$

Equation 8 is the expression for the probability of finding a fragment of length l_i and depends on three coefficients to adjust. In this case we can apply this expression to fit it to the experimental data reported in.[1], where methods of atomic force microscopy were applied to measure FSDF of irradiated DNA.

Figure 1 shows the experimental results for DNA breaking with electrons at doses of 5000 and 7000 Gy. Both are fitted with Eq. 8. Figure 2 represents FSDF for DNA breaking with neutrons at the same doses. In both cases the length of the fragments was normalized to the length of the largest one, and the number of fragments was normalized to the total number of fragments. As it can be seen, the agreement is very good.

More experimental data for electrons from 50 to 200 Gy and neutrons at doses of 900, 7500, 2000 and 10000 Gy were also fitted with good results. In this paper we are reporting the results of the coincident doses of electrons and neutrons of 5000 and 7000 Gy to illustrate the application of this viewpoint. Only in the cases of very low doses of electrons (50 and 100 Gy, where fluctuations in FSDF are important) the results are not as good as the ones before.

This fact reveals the non extensive nature of DNA breaking, as it was shown for macroscopic objects in.[12,13] So, This characteristic of breaking is not exclusive of macroscopic bodies.

Use of Boltzmann´s entropy to describe FSDF obtained in these experiments leads to incorrect results, (*i.e.*,) impossible to fit with the data, which shows power law behavior.

On the other hand, this non extensivity may also reflect an intrinsic nature of the very DNA chain. The presence of $1/f$ spectrum in sequences and long-range correlations in the DNA sequences[14] supports this assertion.

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A. Figure Captions

Fig.1: Normalized DSDF for electron irradiation of DNA at 5000 Gy and 7000 Gy. The solid squares represent the experimental results at 7000 Gy and solid circles at 5000 Gy. Fitting was made with Equation 8. Solid curve is for 5000 Gy. Curve with open squares is for 7000 Gy.

Fig. 2: Normalized DSDF for neutron irradiation of DNA at 5000 Gy and 7000 Gy. The solid squares represent the experimental results at 7000 Gy and solid circles at 5000 Gy. Fitting was made with Equation 8. Solid curve is for 5000 Gy. Curve with open squares is for 7000 Gy.

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