



GLOBAL JOURNAL OF SCIENCE FRONTIER RESEARCH: I
INTERDISCIPLINARY

Volume 20 Issue 2 Version 1.0 Year 2020

Type: Double Blind Peer Reviewed International Research Journal

Publisher: Global Journals

Online ISSN: 2249-4626 & Print ISSN: 0975-5896

' $\frac{3}{4}$ Law' Revisited in Allometry

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GJSFR-I Classification: *FOR Code: 029999p*



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I. INTRODUCTION

Mathematical modeling is powerful tool to test new hypothesis and stimulate dynamic experiments. In addition to simulation it can reduce the dimensions of observation to actually useful set to generalize the data into a meaningful equation. Sometimes modeling is required to harmonize across many systems otherwise specifically to a system in understanding the fine spectra of the observations.

In connection to the mathematical modeling, ontogenetic modeling of growth is a well studied subject. Several models have been developed in order to describe growth of biological systems. Though ontogenetic growth is a non linear phenomena and complex process, yet the studies contributed by West et al in harmonizing across the living world remains exemplary. West et al [1] used fractal like branching of network for the transportation of resources to derive a differential equation showing growth of biological masses. In another approach by von Bertalanffy [11], stated that the energy consumed by an organism is considered to be proportional to the surface area of the body of an organism. Guiot et al [4] extended West's findings to explain the dynamics of solid tumor growth in

vitro with considerable success. Thus we find the applicability of West's general model for the ontogenetic growth of living organisms fits the modeling of solid malignant tumors.

In spite of this success, the infamous $\frac{3}{4}$ exponent [5] is still a mystery in the deduction that applies in the matching of the datasets from single to multicellular organisms.

In the present communication the endeavor is on the understanding of the ' $\frac{3}{4}$ law' conjecture, which is arguably the finest open problems in mathematical biology. The organization of the work starts with Introduction followed by Smoluchowski equation, The Model, then the conception Dynamic Biological Mass followed by Discussions and finally conclusions and future work.

a) Smoluchowski Equation

In reference [7] the authors Hall and Miyake stated that 'Condensations are the aggregations of cells from which cartilages and bones form during embryonic development and from which chondrogenesis and osteogenesis are initiated during repair and/or regeneration.' which means West's assumption is coupled up with a process called condensation. In another reference [8,9] the same condensation like process is reported inside the cell and is discussed in detail in section 2. As stated earlier the growth process is a complex and non linear phenomena, the choice of Smoluchowski Equation to explain the condensation by aggregation is obvious. It is also reported that the condensation by aggregation can only be explained by stochastic theory for capturing the non linear phenomena [2,3].

Typically the non equilibrium process is represented by rate equation. Smoluchowski Equation for the irreversible aggregation is represented as

$$\frac{\partial c(x,t)}{\partial t} = -c(x,t) \int_0^\infty K(x,y) c(y,t) dy + \frac{1}{2} \int_0^x dy K(y, x-y) c(y,t) c(x-y,t) \quad (1)$$

here the kernel is $K(x,y)$ is symmetric wrt to this argument and it determines the collision time which the particle of size x collides with other particle of size y and they merge into a particle of size $x+y$. For the class of kernels $K(bx,by) = b^\lambda K(x,y)$. The exponent λ has some physical significance to this particular problem, if $\lambda > 1$ the gelation process starts accompanied by the non

equilibrium process. This gelation process mimics the formation of biological mass.

b) Model

Initially [2,3] we assume a considerably large number of spherical particles suspended in the fluid medium. These particles experience Brownian motion and are continuously growing in sizes in a heterogeneous medium. As the size increases the weight also increases, in other words, the mass growth

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is directly proportional to the size. To summarize the steps of the gelation process is

1. Two particles are picked at random which exhibits Brownian motion in three dimensions
2. The sizes of the particles are increased by the fraction α of their respective sizes.
3. The sizes of the formed particle are now the present particle.
4. These steps 1 to 4 are repeated up to Infinitum.

The tree structure represents the graphical view of the abovementioned process.

II. DYNAMIC BIOLOGICAL MASS

The basic law due to West et al [1] states that the metabolic energy produced is distributed partly for the maintenance of tissues and other for the generation of the cells. While using the metabolic energy for deducing the ultimate classical sigmoid equation, the process responsible for the generation of metabolic energy is not put to use. The entire motivation for the deduction of the $3/4$ exponent is based on the reports from Princeton University[8,9] and [7]. The opto Droplet reported how proteins inside a cell will assemble into the liquid and gellike states. And also this reversible mechanism to condense and dissolve the proteins by turning the lights on and off. This reversible process is all about the phase transitions (liquidgel). It also reported that if there is an upset in the parameters for the reversible cycle, the process can be irreversible as well as forming solid like aggregates.

As the prime focus is on the reversible process in which the state of the system is acted diabetically without actually undergoing phase transition that results in a state which is less stable than the state if the phase transition would have occurred. So in a generalized way, the cells taken into consideration will exhibit this process. Now we can consider this metastable state as $m(R,t)$ as Dynamic Biological Mass (DBM). In this present communication, we introduce the concept of DBM to differentiate between the real biological mass to have a better understating and spectral of the mass under consideration in [1]West et al's paper.

So by integration of equation 3 and using equation 4 we have,

$$m(R,t) \sim \frac{2t^{4(2a+1)}}{3} - \frac{1}{3}t^{2a+1}e^{\frac{-R\sqrt{3}}{t^{2a+1}}} (2k^3 + 2\sqrt{3}k^2R + 3t^{2a+1}R^2 + \sqrt{3}R^3) \dots(5)$$

Note that the above expression can be seen as the dependent on time.

Now considering the second part of the equation 5 and expanding the exponential expression and considering the term independent of time ($t^{(2a+1)}$), we have,

$$m(R,t) \sim \frac{-1}{3}R^3t^{(2a+1)} \left(1 - \sqrt{3}\frac{R}{t^{(2a+1)}} + \dots \right)$$

Its clear from the system described for a single cell is applicable for a system of cells which is an example of aggregation of the particles whose behaviors are the characteristic of non-equilibrium processes. Thus one can conclude that the process responsible for the growth mimics the condensation due to aggregation physically. In this type of system, any standard theoretical framework developed based on statistical mechanics is found insignificant. This system of non equilibria is generally understood by stochastic theory. In section 1.1 and 1.2 describes the used of Smoluchowski solution of the condensation driven aggregation (CDA) as given by Hassan et al [2,3] for one dimension is

$$c(x,t) \sim \exp\left(\frac{-x}{t^{1+2a}}\right)t^{-2-2a} \quad (2)$$

Now by using [10] extending to three dimension we can convert the above expression for three dimension and using the identities $x^2+y^2+z^2=r^2$ and the inequality $x^2+y^2+z^2 \geq xy+yz+zx$ we have

$$c(r,t) \sim r^2 \exp\left(\frac{-r\sqrt{3}}{t^{1+2a}}\right)$$

this equation represents order of the concentration of masses due to CDA.

Hence the total number of particles should be.

$$dN(t) \sim r^2 \exp\left(\frac{-r\sqrt{3}}{t^{1+2a}}\right) \cdot r \cdot dr \quad (3)$$

While framing the dynamical biological mass formation, the number of particles is considered as the order of mass (considering the mass of each cell as constant). Hence one can write,

$$m(r,t) \sim N(t) \dots\dots\dots(4)$$

where $N(t)$ represents the number of particles.

simplification the above terms generates a term independent of time ($t^{(2a+1)}$), (other terms are not considered as they contain the 't' component)which has the power of 4 as described below

$$m(R,t) \sim \frac{1}{\sqrt{3}}R^4 \dots\dots\dots(6)$$

using the the radius relation to density and mass as

$R = \sqrt[3]{\frac{3M}{4\pi\rho}}$ in equation 6 we have,

$$m(R, t) \sim M^{\left(\frac{4}{3}\right)} \quad (7)$$

Finally changing sides we have

$$M \sim m(R, t)^{\left(\frac{3}{4}\right)} \quad (8)$$

The interpretation for the equation 8 is the real biological mass (RBM) is $\frac{3}{4}$ power of the meta stable DBM, which explains the $\frac{3}{4}$ exponent for the west et al theoretical deduction [1,6].

III. DISCUSSION

The above sections introduce a concept of dynamic biological mass (DBM) and real biological mass (RBM), this hypothesis throws some light upon another part of West et al fundamental consideration that the product of the number of cells produced and the mass of each cell is equal to the biological mass. Practically the number of cells produced must be greater, but due to the evolutionary process, the fittest cells survive and will grow.

Now considering the West et al fundamental equation replaced by DBM in the place of simple biological mass, the equation becomes more meaningful for understanding the evolution process. The report by Guoit et al [4] predicts that the growth of cancer follows the west et al [1] $\frac{3}{4}$ law which can be understood in better terms if DBM with higher-order terms is considered.

IV. CONCLUSIONS AND FUTURE WORK

The hypothesis of using DBM is logically effective in understanding the evolutionary process and if used in cancer growth phenomena then the analysis of fine growth of malicious structures can be identified. This concept can be even extended to distinguish between good growth and bad growth. In the study reported by the Opto Droplet tool reveals that there is an irreversible reaction which leads to the accumulation of solid gels indicative of some unwanted growth.

The future work will be done in the direction of understanding the fractal nature in the process considering the hypothesis is tested.

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