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THE BRAVE NEW WORLD OF BIOPHYSICS: A WORKING-GROUND TO UNDERSTAND THE MICROWORLD

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ABSTRACT
Both the weight and the role of most scientific work depend on finding internal or external properties of any matter, especially 'physical'. The development of scientific world through this dependency on physics has gone to great lengths in acquiring answers to most of human's fundamental questions. The last two hundred years, beginning with the pioneering works in mechanics have provided several examples in which physicists always showed their willingness to go a step farther than the familiar boundary, again quite physically. Especially since the whole of nineteenth century, physics as the basic foundation for any other science has been domineering. Physics support in other sciences has reached a stage where accepting such support became inevitable. However, the dominant physics has slowly turned into a subject 'behind the screens' of the performance of every other science, more successful recently in the field of biology. The world famous pair Crick & Watson and their success can be claimed to be one of such works. Although physics has been the cause for a variety of scientific exploration triumphs, the reductionist view always acknowledged the field of science where physics made the major contribution. This paper dwells on the roles played by the most focused fascinating interdisciplinary science, 'biophysics'; especially, the contribution of physics to it.

KEY WORDS: Emerging Science, Biophysics, Physics Applications

INTRODUCTION

The study of biophysics began much earlier in human history than known. This beginning was a result of human thinking shift from knowing the macroworld toward understanding the microenvironment. Starting from Heraclitus of 5th century BCE, who began the era of mechanistic theories of dynamics of life, biophysics gave us a torrent of knowledge regarding the behavior of microcosm. Leaving the works from Heraclitus time to the fourteenth century, Leonardo da Vinci, the genius, was among the next frontier scholars who worked on rudimentary biophysics through his primal investigation on the basic principle of bird flight, which was in the later years termed as 'bionics', and mechanical principles of working of human heart (Glazer, 2001). A hundred years later, Alfonso Borelli, yet another Italian biophysicist came forth studying the same field of bionics. He also founded a school of iatro-physics (medical physics). Furthermore, eminent scientists Luigi Galvani, Alessandro Volta, J. R. Mayer, Lavoisier, Laplace and others until Helmholtz pioneered the physics-platform for biology opening up an arena of focused interdisciplinary sciences.

Taking modern physical methods and devices as a viable tool for many contemporary experimental findings, biology began to stand out among all the sciences in the last seventy years; particularly as a result of giving heed to learn and manipulate the environmental, human health and societal issues. Quite recently, though time is relative, Erwin Schrödinger (1887-1961), world's invincible physicist who contributed in revolutionizing and transforming the entire face of physics into a new '*uncertain*' quantum reality, opened new gates to encourage physicists toward biology and vice versa, through his fascinating article "What is life?" His vivid but brief explanation on "organisms come into existence via the concept of cell division – mitosis" with a quantum mechanical evidence led to a rapid development of biophysics as an interdependent science (Schrödinger, 1944). Recently, biophysics also joined the league of sciences that could aim an arrow at the infamous Global Warming target, in the name of Environmental Biophysics.

Cell division was explained by Schrödinger in biological terminology; it was an opportunity to see the same concept in physics terminology. Reference can be made, in this context, to Thomas Mann of The Magic Mountain. In his words, "What then was life? It was warmth, the warmth generated by a form-preserving instability, a fever of matter, which accompanied the process of ceaseless decay and repair of albumen molecules that were too impossibly complicated, too impossibly ingenious in structure. It was the existence of the actually impossible-to-exist, of a half-sweet, half-painful balancing, or scarcely balancing, in this restricted and feverish process of decay and renewal, upon the point of existence. It was not matter and it was not spirit, but something between the two, a phenomenon conveyed by matter, like the rainbow on the waterfall, and like the flame" (Mann, 1985).

Physics of the *Double Helix DNA*

February 1953 remains as one of the miraculous times of historical human scientific exploration endeavors. One woman-physicist, Rosalind E. Franklin, remained the basis to find the '*secret of life*'. James Watson and Francis Crick, the esteemed pair of biochemists used Franklin's X-ray Diffraction data "for their discoveries concerning the [Nobel Prize winning-] molecular structure of nucleic acids and its significance for information transfer in living material," (Elkin, 2003) – the soul of the chain of heredity.

For this work, Franklin is remembered as one of the path-finding biophysicists of 20th century. The ***double helix*** was claimed to be the shape of DNA in chromosomes through the results in the experiment where crystalline DNA from the thymus gland of a calf was diffracted by X-rays. This way, Watson & Crick scientific duo led the human race involve itself in the renowned *Human Genome Project*. This industrious undertaking exemplifies the hallmarks of physics applied in biology, reminding us of the brave new world of *biophysics*.

BIOPHYSICS DEFINED

The word biophysics emerges from multiple ideas, fundamental questions and scientific inquiries (Nelson, 2004). While some researches show that this subject came up from the scientists who were intrigued by the physical behavior of heat, others say that it all began with the human curiosity to find the ways to see within human body. In his book on Biophysics, one of the contemporary researchers in the field, Rodney Cotterill notes that "it is probably no exaggeration to say that many regard biophysics is a discipline still waiting to be adequately defined." However, according to his 'unified picture emerging' from many ideas such as mentioned above, "***biophysics is the application of physics to biology, with a view to furthering the understanding of biological systems***" (Cotterill, 2002). One reference is found very common in most of the works in this field that, it was the scholar Karl Pearson who coined the term biophysics in 1892 (Glazer 2001). Nevertheless, many scholars in the field tried to give a general overview of biophysics in a few phrases such as the one given above. In short, it is a radical new field of interdisciplinary science that applies the laws and theories of physics to questions of biology. Plainly speaking, the laws and theories of physics revolve around understanding the phenomenon of matter and energy associated with it; particularly in the living organisms is the key focus of this novel subject (Goldfarb, 2011). Furthermore, biophysics takes as its sisters the other most fundamental sciences: chemistry and mathematics; while its cousins appear as and when necessary: anatomy, physiology and climate studies.

In order to best view the actual purpose of biophysics, it is quintessential to understand a few cardinal and underlying concepts of physics. As already mentioned, physics is the scientific inquiry into everything that consists of matter and energy and how they interact with each other. Specifically, energy embodies itself in the form of motion and gravity, light and electricity, radiation and blackbodies, and owing it to Albert Einstein, in the form of mass as well. The current framework of Physics covers a vast portion of this universe such as: the particles living within the elementary particles such as within protons and neutrons (neutrinos, quarks, etc.), molecules, all solids and fluids, stellar objects like stars, galaxies, blackbodies, etc. and everything in between.

Remembering that the most fundamental sciences which laid the solid foundation for today's technology innovations are biology, chemistry, mathematics and physics; physics has an undeniable distinctive attribute for it prepared an essential framework for the other three sciences leading them towards finding answers to many fundamental questions. The terms came in existence through these endeavors are chemical physics, mathematical physics and biophysics. Although physics urges to exploit all that are observables (especially, quantum physics) (Krishnan, 1994), it is now spreading into some incredible subjects like psychology unleashing the new *psychophysics*, realizing the often complex psychological operations in the brain as observables. (One can refer to the upcoming *econophysics* as well, physics applied to economics.) There is an immense amount of healthy debate between biophysics and psychophysics (Mather, 2009): especially with key concepts such as foundations of sensations and perceptions where both can be viewed from the standpoints of biophysics and psychophysics with different sets of perspectives.

At all levels, biophysics explores the complex biological processes that involve understanding and manipulation of micro environment within the living organisms. Also it is biophysics that supplies both physical tools and formulas to interpret and handle a genuine biological problem (Lipanski, 2010). Further, biophysics is micro world science. It studies biological systems in terms of multi-atomic particles, mainly molecules of size ranging between 1 nm (fatty acids and sugars) to 5-10 nm (proteins) and up to greater than 1000 nm (starches). Consider a human being. The machines which keep a human body functioning are called as cells. There are countless cells in a human body. Inside a cell, there are countless biomolecules such as DNA molecule (deoxy-ribo-nucleic acid). This DNA molecule, if extended, is about 45 miles long but only 2 nm thick. That's where biophysics works.

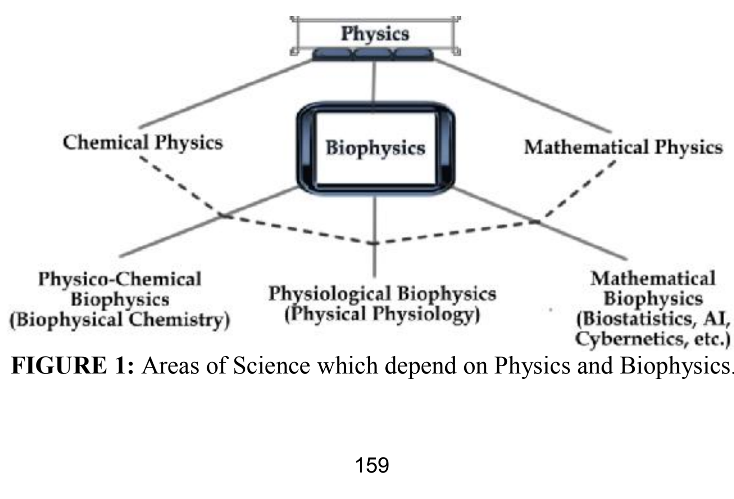

FIGURE 1: Areas of Science which depend on Physics and Biophysics.

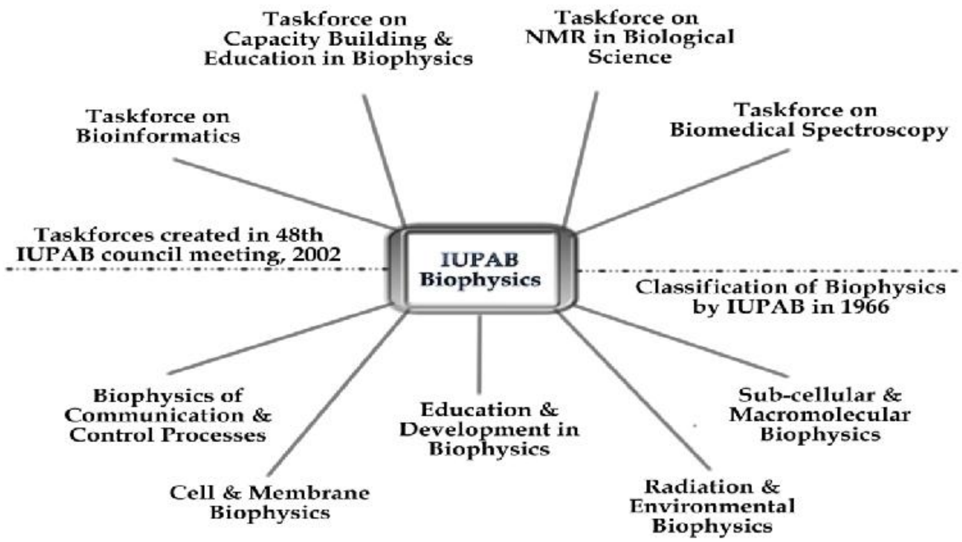

FIGURE 2: Classifications and taskforces of Biophysics as per IUPAB

The most fundamental sciences depend on physics for foundational advancements. Especially, biophysics uplifted more exceptional resources for scientific and technological challenges, thereby possible resolutions and probable further consequential questions. Hence the new challenges resulted by physics expanded the contribution of biophysics in the task of comprehending several empirical and theoretical hypotheses continually roused both in classical and modern subjects. Here classical subjects refer to physiology and anatomy, biochemistry and physicochemical analysis, etc. and modern are computations for understanding biological systems, taking-a-step-further of revolutionary artificial intelligence (AI), bioinformatics and cybernetics etc.

This ontogeny of biophysics triggered the International Union of Pure and Applied Biophysics (IUPAB) to institute taskforces during the 2nd International Biophysics Congress in 1966 (Gohary, 2006). According to these taskforces, biophysics is targeted to impact: 1) Bioinformatics; 2) Capacity Building and Education in Biophysics; 3) Nuclear Magnetic Resonance (NMR) in Biological Science; and 4) Biomedical Spectroscopy

Where do Biology and Physics Meet?

Dimensions

Physics deals with any matter, whether subjective or objective, primarily through measuring and attributing some units and dimensions, such as length-mass-time scales, velocity-force-energy scales, and many derivatives (Newman, 2011). These range enormously between the micro scales such as nano, femto, pico scales and macro scales such as light years at quintillion scales. Biology, on the other hand, involves itself with questions dealing with scales lying in nanometer to a few meters range. At this common field, physics lays the platform for biologists' study.

Space-Time

Also, all biological systems, perhaps any system, functions within the framework of space-time. Especially physics would not be able to uncover any description of such a system which is beyond the norms of space-time. This could be one of the reasons why physicists are driving themselves strongly towards understanding the practical behavior of black holes. Biological space-time limitation gives the right access and ease to physics to find out the structures and dynamics of systems within.

Entropy

Concepts relating to statistical ensembles physics, heat exchange between molecules, and phenomena relating to unconventional electrical conductivity and many others depend on comprehending the responses of particles while forced to or not to cross a particular barrier line, called as membrane. Usually, the matters of equilibrium are studies of examining the particle kinetics on both sides of these membranes. Any system which is not in equilibrium will instantly become a topic of extensive interest for physicists. This randomness, called as entropy in any system, is a direct result of sub-systems not being at equilibrium with each other or with their immediate surroundings. This disciplined randomness is essentially a feature of biological systems. Physics plays the key role in bringing these systems to clarity, though not back to equilibrium. Within the same concept lies the dependency of (any) systems on temperature-pressure-volume standardization conditions.

Electromagnetism

Since any system in nature is necessarily physical, energy is the undercurrent factor that fits natural systems in the known 'orderly' edifice. In the case of particles such as atoms, molecules, electron-proton pairs, uncharged particles, molecular combinations, all rely chiefly on the effects of energy absorbed by them. After the triggered practice of analyzing systems quantum mechanically, information about these particles unambiguously depends on the interaction of radiation (electromagnetic energy) with material particles, like the ones found in biological domain. Electromagnetic energy has been a subject of physics so vast and the only subject seemingly thoroughly understood, that its applications array all the way from a bulb to a bulldozer, from a literal 'atom' (referring to its meaning – *'further indivisible'*) to the edge of the universe, and perhaps beyond.

Studying the response of these tiny particles to the incident electromagnetic energy is called as spectroscopy. Most advances in medical diagnostic and imaging fields are a direct result of electromagnetic interaction of biological particles/systems. Rontgen's experiment of imaging the skeletal frame of his own hand is one of the primitive examples.

Similarly, a proton's behavior in a magnetic field, interpreting its response to the field in terms of its spin and precession led to the birth of nuclear magnetic resonance (NMR). Using the same phenomenon, the advancement took place in the form of Magnetic Resonance Imaging (MRI) which is widely used in all parts of the world now. To further the application of the same concept of NMR, physicists discovered NMR spectroscopy to study the behavior of many chemical and biological elements.

Several other factors

Most briefly, the above mentioned elucidate only some, but significant, of the domains where physics meets biology. Recent advances in physics techniques and the accumulation of tremendous amounts of experimental data given by these techniques allow for posing and addressing fundamental questions of biological systems even more deeply.

Overview of Biophysics Applications

Biophysics serving the biomedical sciences has reached its peak with the pioneering works of Hans Frauenfelder of University of Illinois. "Life is based on biomolecules" (Frauenfelder, 2010). After his discovery of perturbed angular correction (PAC) of nuclear radiation, Frauenfelder initiated applying physics to biological systems, particularly to measure how proteins response to excitation by a light photon which leads to higher temperatures.

While biomolecules play an important role in biologically understanding life, biophysics plays an important role in physically understanding the dynamics of biomolecules. Among these biomolecules, proteins stand out as the labor behind the cellular actions and activities. Biophysics is becoming an established approach for biomolecules structure determination and has been the largest contributor in taking biomedical sciences to new profundity, for example: being able to visualize the structures of proteins through protein building blocks, finding particular reasons for their structures and successions, analyzing their specific functions, up to manual manipulation of proteins through unraveling them and connecting them back with add-ons, and the work is in further progress. Among these, the most widely spread research work is on protein-folding, "the holy grail for the structural biology community" (Koehl, 2012).

The atomic physicist, Alexander Jablonski, the father of fluorescence spectroscopy, through his original first-hand experimental findings contributed to the entire world of biomolecules (Lakowicz, 2006). Currently, research works in biomedical engineering and physics using fluorescence spectroscopy to study biomolecules like proteins has become one of the widest-scope scientific career options. Considering studying Joblonski pictures is known as the primary step in analyzing absorption and emission of a certain electromagnetic radiation. Using fluorescence spectroscopy, there is numerous studies on protein-folding and function manipulations.

With the advent of computer technology innovations (again as a result of physics applications), the scientific analytical dimension has taken a fresh turn towards Molecular Dynamics, modeling and simulation methods in biomolecular applications. The concept of molecular dynamics is based on the theory that any biological system comprises of micro particles, called biomolecules, and their dynamism follows physical laws of motion (Dickey and Faller, 2012).

Apart from the continuous efforts of biophysics intervention in medical and physiological sciences through research studies, the increasing sophistication in medical imaging methods, non-invasive diagnostic innovations is clear. The well-known biophysics book, *Physics of Human body*, by the physicist Irving P. Herman begins with, "physics explains everything from the beginning to the end of any complete description of the human body" (Herman, 2007).

For instance, although not intending to limit the talk to human alone, one of the data that biophysics has shown is that blod flows in human body because it has its metabolic needs (Zamir, 2005); from this stage, biophysics worries about issues such as: What must be the temperature consistency in the blood, how its changes affect? What happens if the blood velocity falls to a threshold level or beyond? How blood fights against and makes use of gravity simultaneously? What if blood cells collected a few wrong air molecules from the lung activity? What if the synergy between the functions of lungs and heart ceases for a fraction of a second?

The functioning of a human body requires a variety of intermolecular interactions, principle functioning of biomolecules like cells and proteins and all these activities leading to mechanisms of signal propagations. Every single part of the body requires to be incessantly directed through signals generated and received by brain. Brain plays a vital role in our body's every activity. Understanding the most complex neural networks inside the brain and exploring their every single function involves almost all the predominant topics of physics. Brain interacts with each other body part, how much ever smaller it is, in a highly specific manner and selectively recognizes its beneficiaries and working partners among the billions of neurons (nerve cells) inside. Analysis of the underlying mechanisms and key factors in brain's recognition and direction process is essential for the predication of minute details of body activity.

Recent technological advancements permitting identification of methods involved in brain activity of diverse molecular and nervous properties and consequently brain's level of quantitative reasoning are attracting physicists to study the biological system of brain.

It is through physics that one infers that the activity of brain demands continuous impulses of electrical and mechanical disturbances through nerve cells, called *neurons*. A neuron leaves a few branches out of it, called *axons*. Each nerve undergoes a continuous disturbance produced by electrical signals throughout the length of its axon. The electrical signal so produced lasts for a millisecond and with a potential of 50 millivolts. Due to these electrical signals, the molecular orientation is affected within the axons producing mechanical disturbances (Neumann, 1986). These disturbances carry forward the information in the form of signals to the rest of the body, producing continuous electrical and mechanical disturbances in human body; and thereby a perfect communication system of brain.

The above explanation is the fundamental concept of brain that scientists believe that they are well aware of. As of now, we only know fairly thoroughly about how and what in brain communicates with the rest of the body and surroundings (Schwartz et al. 2004). Neurophysicists have been successful in acquiring good working knowledge of the role of brain in processing complex information and communication with its partners and nature. However, the question of why it so behaves is the actual challenge for physicists to crack and they are working on it presently. Also, biophysicists seem to take exceptional research interest in finding the contradistinctions and contradictions between mind, brain and consciousness (Benerjee and Chakrabarti, 2008).

Biophysics has been largely contributing in the area of sustainable agriculture. One of the many definitions of sustainable agriculture is given as, "it is a management system for renewable natural resource for food production, income and livelihood for present and future generations, maintaining and improving economic productivity and the ecosystem" (Vasilevski, 2003). It is statistically proven that agriculture, especially crop enhancement, achieved many heights such as: seed germination increased from 20 to 35%; vegetative mass increased from 10 to 45%; increased resistance from drought; etc. According to the researchers in this area, the agricultural research has taken a redshift in exploring application tools from chemical resources to physical tools and methods.

In terms of improvising the optical tools for medical diagnostics and other technological innovations, biophysics is currently giving a torrent of opportunities through its torrent of most advanced tools like lasers. Human Breath analysis using Cavity Ringdown Spectroscopy (Wang et al, 2008), photovoltaic cells research using fluorescence spectroscopy (Fuini JF et al 2010), green fluorescent proteins research for biological imaging (Shanner et al 2005); biophysical methods for climate and ecology studies (Helmuth, 2002) are some of the novel millions-of-dollars patent works in biophysics.

Biophysics Challenges

The Committee on Research at the Intersection of the Physical and Life Sciences of National Academy of Sciences (USA) has divided the tasks to address scientific problems lying at the intersection of the traditional areas, physics and biology (O'Shea, 2010). According to their division outline, some the most important challenges to be faced by biophysicists can be summarized as:

1. Grand Challenges:
   - Neurophysiological challenges
   - Ameliorating Data collection of individual organism's characteristics from their DNA sequence
   - Interactions of the earth, its climate and the biosphere
2. Societal Challenges:
   - Medicine, imaging, treatment and devices
   - Agriculture as a resource for food and energy
   - Identifying and combating biological threats
3. Innovation Challenges:
   - Technologies and tools for knowing physical basis of molecular recognition
   - Creating connections between scientific disciplines enabling the research at the 'intersection'
   - Improving Academics enabling the research at the 'intersection'

From Unknotting to Knotting: Biophysics Integrating Sciences Back

This small section very briefly displays the power of biophysics in a new dimension. While the whole scientific world has begun its work with simplifying philosophy by dividing it into different subjects, and further simplifying natural sciences into Physical and Biological sciences, here is the new biophysics which is constructing a latest and sophisticated intellectual cross roads where sciences come back and join their hands together towards one common goal. The authors would like to strongly recommend a book showing this remarkable feat of biophysics which is highly intensified with knowledge, "Life in the Universe" by Dirk Schulze-Makuch and Louis N. Irwin of Washington State University and the University of Texas at El Paso, respectively. This 2008 edition volume is a part of the series called Advances in Astrobiology and Biogeophysics (e-ISBN: 978-3-540-76817-3), by Springer Publishing Company, Heidelberg.

CONCLUSION

The information given in this paper may not conclude the list of possible applications or the amount of defining information materials in biophysics. But this can trigger some serious thinking of the importance and significance of such a brave new multidisciplinary subject for the environment and learning communities in the developing countries. The usage of this subject in the production of scientific human resources will enable intense benefits for all the concerned from the communities to the governments. Surely wider acceptance of biophysics as being faced by the greatest challenge of designing the necessary essential physical tools and apparatus for biological study is wide spreading. However, it is a great honor to keep tracking the growing synergy between physics and other sciences for any physics learner.

RECOMMENDATIONS

1. Targeting this work mainly at the aspirants belonging to the developing countries like India, it is essential that the public and private agencies should improve the multidisciplinary studies and the students must be given awareness and inclination towards such academic and research work right at their higher secondary school education.
2. Public and private universities and educational institutions must further their international collaboration especially in the case of academics and

research in biophysics. At this time, in India for instance, there are only a handful of public institutes encouraging learners into this promising area.
3. The engineering and technology institutions (in India) must focus on adding and designing engineering biophysics as one of their curricular domain. The educational institutions in many developed countries can be found with special department dedicated for Engineering Physics.
4. Public and private funding agencies must increase scientific proposals that involve scholars from a variety of scientific disciplines and aiming a research project involving a variety of sciences such as: physical sciences and biological sciences.
5. Private sectors should amend their investment policies and their usual way of hi-tech and most attractive marketing strategies must be implemented in a way, that they can innovate science centers in the communities luring students to join and explore the global science and global opportunities in the field of biophysics.
6. Institutes and universities where biophysics is already made a part of their curricular interests must increase the number of workshops and conferences also majorly for the general audience who has the hope and potential to enter the field of biophysics.
7. In the case of medical diagnostics, as the world is moving fast towards non-invasive tools, it is of high importance that institutes carry out academic and research designs in this field using biophysics.
8. On the learning side, the authors recommend that a learner aspiring to take up the field of biophysics be well equipped with the prerequisite Nuclear Physics.
9. Also, most biophysics learners face the problem, especially those dealing with biomolecules and chemical physics, of tedious biological terminology. The book given in the references section called "Physics of Human Body" by I. P. Herman begins with very easy and learner-friendly details of how to memorize the heavy biology terms.

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