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Review Article

The Complexity of Dissolved Oxygen Levels Assessment and its Biochemical Interpretation in Biological Fluids

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Abstract

Dissolved Oxygen (DO) has a key role in cellular metabolism. DO levels are measured to identify pathological conditions, try to explain pathophysiological mechanisms, and monitor the efficacy of therapeutic approaches. This is particularly relevant when the measurements are performed in vivo. Biological fluids and synthetic clinical fluids represent a challenging environment where DO interacts with various compounds and can change continuously and dynamically.

Keywords: Atmosphere; Cell; Energy; Fluids; Hypoxia; Hyperoxia; Indicator

Introduction

Oxygen (O_2) is one of the fundamental molecules of life, playing a major role in cellular metabolism. O2 has a high redox potential making it an ideal electron acceptor and, therefore, a sink for the capture of energy for intracellular use [1]. Supposedly, oxygen is taken up reversibly from the atmosphere and transported to oxygen-depleted tissues, where it is stored until actual use. Circa of 90 to 95% of the dissolved oxygen (DO) consumed by the body is utilized by mitochondria to supply cellular energy through respiration and oxidative phosphorylation [2], however these biochemical concepts are theoretical in their major part, in spite that regulation of tissue oxygenation and maintenance of adequate O2 levels are fundamental requirements for a healthy organism.

Thereby, DO levels represent a significative indicator to evaluate pathological conditions (such as abnormally low or high DO levels, hypoxia, and hyperoxia, respectively) and eventually explain pathophysiological mechanisms and monitor the effects of therapeutic treatments [3]. Several methods for determining DO in the various aqueous and biological matrixes have been developed. The main ones include iodometric titration, electrochemical and optical methods.

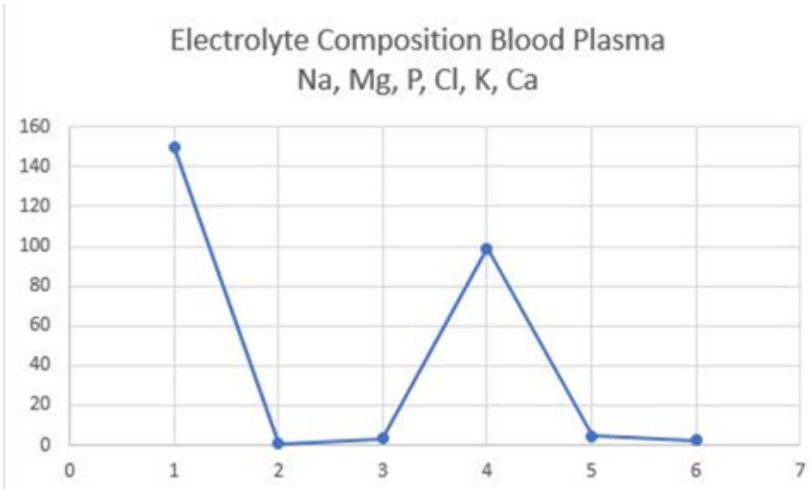
Despite its profound biological and clinical importance, a limited number of effective methods exist for quantifying DO in its physiological settings, and real-time measurements are not always available. Therefore, it is necessary to improve the ability to quantify oxygen levels to further study its profound impact on physiology and diseases [4]. Since oxygen is tightly coupled to the production of cellular energy, low DO levels cause a decrease in the cellular energy state [5], and certainly the dissolved oxygen levels reflect the energetic state of the cell, but because all the oxygen we have in the body, which is equivalent to almost 5 times more than the oxygen levels in the atmosphere, comes from the dissociation of the oxygen molecule. water, as in plants [6].

As much as glucose is considered the energy source par excellence in biology, and inasmuch it is a concept deeply rooted,

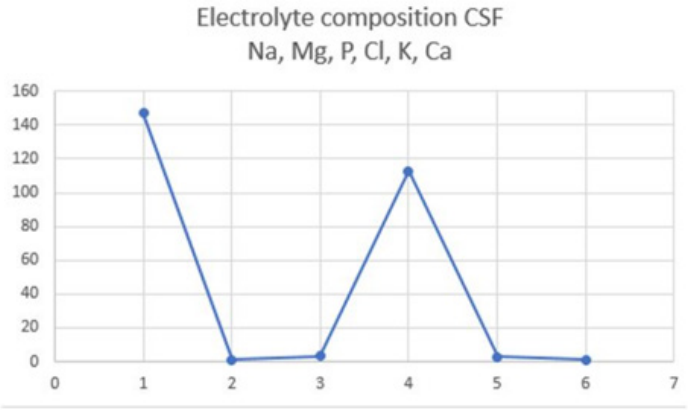
finally it just keeps being a model that has even become dogma but so far, it is not possible to position it as a high-level theory. Normal oxygenation levels in human organism depend on the nature of the tissue and are affected by inspiration and expiration phases [7]. But it is here that we have another inconsistency in the current model, since the function of the lung is only to expel CO2, and it does so constantly, night and day; but in no way does the alveolar wall have intracellular components that would allow it to separate oxygen from nitrogen, and then concentrate it 5 times above the amount of oxygen in the atmosphere, and finally introduce it into the bloodstream [8].

Extracellular Fluid (ECF)

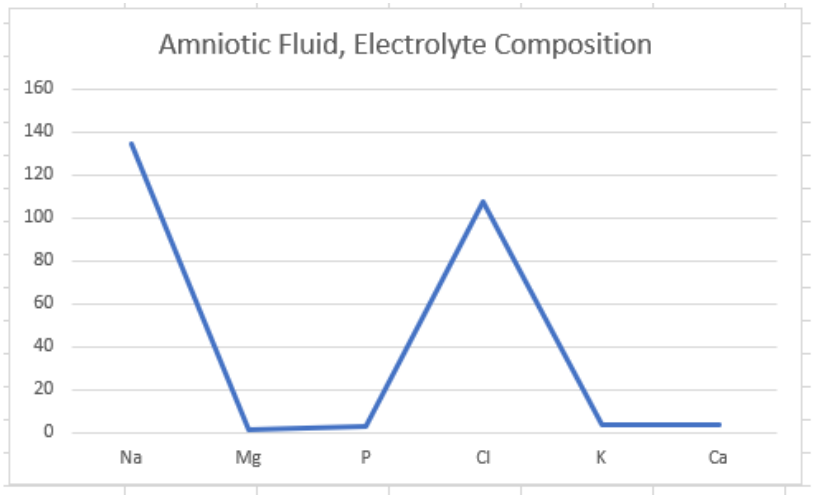
ECF represents 33 % of the total human fluids content and includes: a) Plasma, the liquid part of blood, B) Interstitial fluid, with mediates the interactions between the blood vessel and cells content, (C) Lymph, (D) transcellular fluids, (E) cerebrospinal fluid, and to a lesser percentage synovial and pericardial fluid and aqueous humor [9]. It forms about 14 L (about 20% of total body weight), of which 15% is interstitial fluid and 5% is plasma [10]. Intracellular fluid (ICF): It forms about 28 L (about 40% of total body weight). Another fluid that is a byproduct of the body is urine, and its DO content can also be considered informative [11]. I make a brief parenthesis about the origin of biological fluids, which is a controversial issue, but the graphs below (graphs 1-6), some of them have already been published, show us a remarkable similarity in the distribution of the main electrolytes they contain, which It can be interpreted in different ways, but I would like to point out that this similarity would also speak of a common origin or process (Figure 1-6).



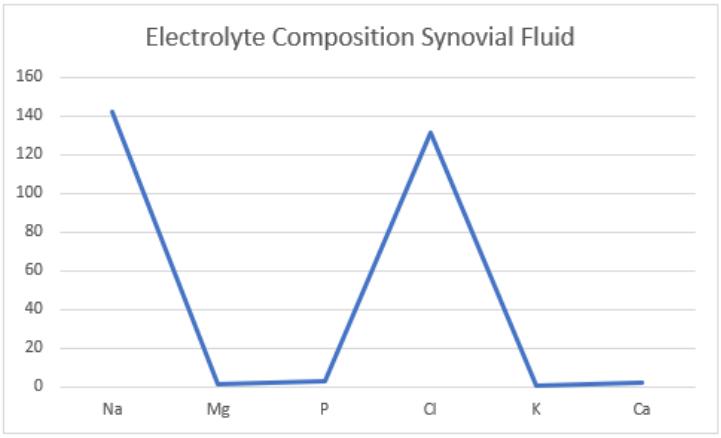
Graph 1: The distribution of electrolytes in the plasma (Sodium, Magnesium, phosphorus, Chlorine, Potassium, and Calcium) has the distribution shown in the graph. The values were taken according to the literature [12].



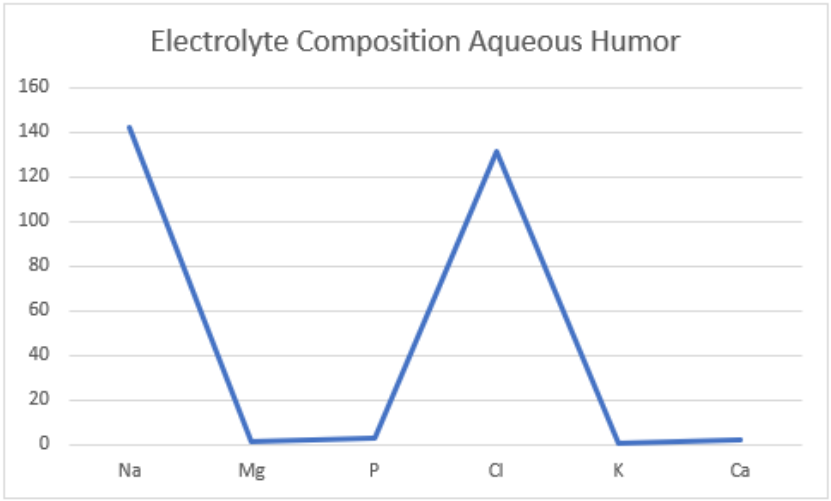
Graph 2: in the case of cerebrospinal fluid (CSF), whose dynamics (production, route, absorption) is controversial, the distribution of Sodium, Magnesium, Phosphorus, Chlorine, Potassium and Calcium, is graphed according to the values reported in the literature [13].



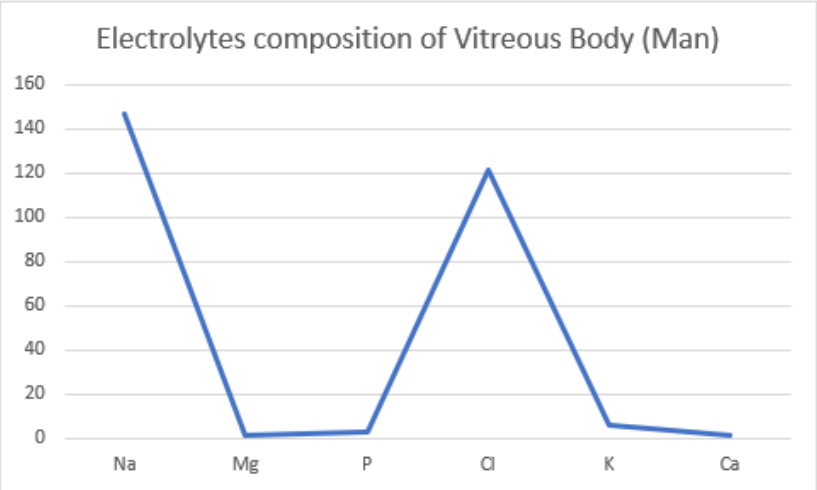
Graph 3: The amniotic fluid has vital functions during the development of the fetus, its origin is controversial, and its composition still has mysteries. The distribution of the electrolytes it contains shows a remarkable similarity with other biological fluids, which indicates a common origin. The values represented were taken from the literature [14].



Graph 4: The composition of the synovial fluid is complex, however the distribution of the main electrolytes it contains again shows a surprising similarity with the distribution of electrolytes in other biological fluids, which could be explained in different ways, in my opinion the common origin seems to be the most coherent. The plotted values were taken from the literature [15].



Graph 5: The aqueous humor has several important functions regarding the nutrition of the tissues of the anterior segment, and of two of the largest avascular and transparent structures in the human body: the cornea and the lens. The origin, absorption and dynamics of aqueous humor are still controversial. The values represented were taken from the literature [16].



Graph 6: The water contained in the vitreous body is not replaced throughout the individual's life, however its physical-chemical qualities, such as dissolved oxygen levels and pH levels, remain within normal limits. The distribution of the electrolytes it contains is surprisingly stable and even more so the similarity of said distribution with that of other biological fluids. The values represented were taken from the literature [17].

Despite the differences between the location and function of the different biological fluids, the distribution of the main electrolytes (sodium, magnesium, phosphorus, chlorine, potassium, and calcium) has a surprising similarity. One might expect significant differences between electrolytes since the functions they carry out, as well as their location, are apparently different. If we start to explain these similarities through imaginative theories, we can write several books, but the common origin is congruent, coherent, if we start by explaining how both liquids and electrolytes are generated.

Returning to the complex issue of dissolved oxygen (DO) as well as the technical difficulties to determine it, and even more so to understand its biological role in the different body fluids, we cite its somewhat tangled nomenclature as evidence: (1) Oxygen content (CaO2) measures the total oxygen content in arterial blood. (2) Partial pressure of oxygen (paO2) measures the pressure of oxygen dissolved in the arterial blood and how well oxygen can move from the airspace of the lungs into the blood. (3) Oxygen saturation (% SaO2) refers to the percentage of hemoglobin binding sites in red blood cells that are carrying oxygen.

If we examine the concepts separately, then we have the following:

(1) Oxygen content (CaO2) measures the total oxygen content in arterial blood.

The total oxygen content in arterial blood is a dynamic process that constantly changes, it is not linear in any way, and even more so because it does not depend on the lungs or the alveolus, in short, the oxygen that we have in any tissue of the body does not come from the atmosphere but from the water dissociation process that takes place in each and every one of the cells of our body. And to top it off, hemoglobin is more than 98% similar to chlorophyll, therefore it also irreversibly dissociates the water molecule, so more than transporting oxygen, hemoglobin generates it by dissociating the water molecule.

(2) Partial pressure of oxygen (paO2) measures the pressure of oxygen dissolved in the arterial blood and how well oxygen can move from the airspace of the lungs into the blood.

This concept needs to be completely modified, since atmospheric oxygen cannot pass through lung tissue, however thin it may be, and reach the bloodstream [12]. It would be more accurate to say that the partial pressure of oxygen measures the intensity or efficiency with which the hemoglobin in the blood is dissociating the water molecule in a patient at a given moment.

(3) Oxygen saturation (% SaO2) refers to the percentage of hemoglobin binding sites in red blood cells that are carrying oxygen.

This concept is as wrong as the previous ones, since hemoglobin does not carry oxygen, it cannot; In fact, the omnipresence of oxygen in the blood reflects the intense activity of hemoglobin dissociating the water molecule, which explains its constant presence, but in no way does hemoglobin capture atmospheric oxygen from the blood and distribute it to the rest of the body through the blood supply.

So % SaO2 also measures the efficiency with which the hemoglobin molecules contained in the erythrocytes are dissociating (irreversible) the water molecule.

The relationship between CO_2, and pO2 arising from the presence/absence of oxygen carriers. But we have that the blood does not carry oxygen, but produces it, so this supposed relationship is wrong, its bases are imaginary, and therefore confusing.

Thereby, the relationships between these parameters are quite complex, this is: very difficult to explain; and a series of farfetched mathematical models have been developed trying to describe them, such as the entirely theoretical Equation proposed by Severinghaus to also try to describe the relationship between SaO2 and paO2 [13].

Furthermore, this already complex background is further complicated as expected, while try to define the concentration limits typical of each clinical state is a nightmare since each cell type/tissue has its own physiological parameters [14]. The composition (thus also DO levels) of biological fluids also depends on a series of parameters spacing from the area and time of sampling to the health of the patient and the objectives of the clinical field and applications. DO concentration in blood is also greatly affected by the phases of the respiratory cycle [15], but this affectation is not due to the gaseous exchange of atmospheric oxygen with the blood through the lungs, but to the fact that the main function of the lung, which is to expel the CO_2 that is continuously formed inside the body into the atmosphere, is the change which actually modifies the production of oxygen within the body and therefore the levels of dissolved oxygen. Therefore, the greater the presence of CO_2, the levels of dissolved oxygen are lower, and vice versa. The CO_2 molecule inhibits greatly the biological mechanisms by which the cells transform the light power into chemical energy susceptible to be used by all living things, through a process that seems is universal: water dissociation. The pigment that gives the color to black molds and fungi is melanin [16]. Thereby, molds do not take oxygen from the airspace, instead of the water they contain inside.

Since the change in the dissolved oxygen concentration in a living being is a continuous and dynamic process [17], high-accuracy, rapid, and real-time DO detection methods are essential for in vivo/ex-vivo measurements. But it is something difficult to achieve as long as we do not break the dogma that the oxygen present inside our body comes from the atmosphere, for more theories and tangled mathematical models that may be proposed.

Thereby, the classical determination methods of DO that include titration (Winkler method), optical methods, and electrochemical methods, they should be redesigned considering the discovery of the unsuspected capacity of the human body to transform the energy of light into chemical energy, through the dissociation of the water molecule, like plants.

Therefore, it is not by chance, that electrochemical DO sensors are now the most widely used sensors since they can perform in situ and online measurements [18]. They can be based on conductivity, potentiometry, or current intensity based on their output signal. Intensity-based sensors, which are the most interesting for DO measurement, can also be divided into polarographic and galvanic types. Potentiometric DO sensors contain an oxygen-sensitive material fixed on the surface of the working electrode [19]. When oxygen molecules are close to the sensitive surface, the working electrode is polarized. The voltage difference between the working electrode and the reference electrode is directly proportional to the logarithm of the concentration of DO, thus allowing its quantification [20]. That is: electrochemical oxygen sensors still measure oxygen, whether it came from the air or from the dissociation of water (Figure 7).

Figure 7: The bubbles coming from water dissociation are clearly visible in this photograph taken from a material developed in basis of human eye biology.

Conclusion

Biological fluids of clinical interest comprise human fluids and a series of solutions exploited in fluid-based therapies. Compared to other fluids where oxygen is routinely measured (e.g., natural basins waters), they are characterized by an overall higher chemical complexity and tendency to deteriorate. The pulse oximeter is a particular kind of optical DO sensor widely used in a variety of clinical settings, including emergency and critical care, and is now often part of standard patient observations. It plays a role in monitoring and treating respiratory dysfunction by detecting hypoxemia and is effective in guiding oxygen therapy in adult and pediatric populations [21]. The principle of operation of the pulse oximeter is based on the different light absorption characteristics of hemoglobin at different wavelengths. The

absorption spectra of oxygenated and deoxygenated hemoglobin are sufficiently different. But now we can think that deoxygenated blood refers to blood with a high CO2 content, which significantly impacts the ability of hemoglobin to dissociate the water molecule, and therefore the greater the presence of CO2, the less water dissociation and therefore less oxygenation, and vice versa. The system works by transmitting and detecting the differential absorption of two wavelengths of light, typically 660 and 940 nm, through thin tissues, such as a fingertip or earlobe; 660 nm light experiences greater absorption by deoxyhemoglobin (higher CO2 content), whereas 940 nm light is more strongly absorbed by oxyhemoglobin (lesser CO_2 content). By measuring the periodic modulation of this differential absorption, due to pulsed blood flow, pulse oximetry isolates the oxygen saturation of arterial blood alone without contributions from other absorbing species, such as venous blood. Pulse oximetry can suffice as a monitoring technique when patients are not affected by the risk of respiratory failure or metabolic acidosis pulmonary diseases. Oxygen monitoring in a biological setting is very faceted, mainly because of liquid specific features, since oxygen content is dependent on the liquid type in which it must be quantified (salinity, temperature, the composition of the solution can affect DO levels). Patient-related features in vivo, since body Temperature, arterial/venous pressures and health conditions affect the oxygen levels. Oxygen level types of classifications, or expressions since oxygen content can be expressed either in absolute or relative measurement units. The type of target expression should be properly chosen, considering the underlying clinical needs and aims of the monitoring. Finally, different sample handling needs based on the location of the source. Once we banish the dogma from our minds about the fact that the oxygen inside the body comes from the atmosphere, and once the knowledge about the unsuspected ability to dissociate the water molecule is spread, we can more adequately interpret the measurements and readings provided by the different current methods.

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Conflict of Interest

No conflict of interest.

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