

The Odyssey of Atmospheric Oxygen in their Futile Attempt to Reach the Interior of the Cell

Arturo Solís Herrera¹ and Martha Patricia Solís Arias²

Abstract

It is possible that the contradictions that emerge when contrasting hypotheses about gas exchange in the lungs with different clinical and experimental findings in both pulmonary and systemic diseases can be solved if we modify in our mind the role of atmospheric oxygen as the main source of oxygen in the blood and take into account both the intrinsic property of melanin to dissociate and re-form the water molecule which is the true source of intracellular molecular oxygen and also the intrinsic property of hemoglobin to dissociate the water molecule that is a significant contributor of oxygen levels in blood. Recall that chlorophyll and hemoglobin are virtually identical, as is the Mg the prosthetic group in chlorophyll and Fe in hemoglobin; another difference is that chlorophyll has a non-polar end that serves to bind to the chloroplast.

Keywords: Atmospheric oxygen, Melanin, Cell.

1 Introduction

There are many concepts about oxygen and its relation to metabolism, which despite being widely accepted, collide with both experimental and clinical findings, not only in the case of diseases but also when we try to explain the normal physiology. Here are some examples:

Traditional view: Mammalian life and the bio-energetic processes that maintain cellular integrity depend on a continuous supply of oxygen to sustain aerobic metabolism. Reduced oxygen delivery and failure of cellular use of oxygen occur in various circumstances and if not corrected result in organ dysfunction and death [1].

¹MD, Ph.D, Human Photosynthesis Study Center, Aguascalientes, México; López Velarde 108, Centro, CP 20000; Phone: 524499160048, 524499150042.

²MD, Human Photosynthesis Study Center, Aguascalientes, México; López Velarde 108, Centro, CP 20000; Phone: 524499160048, 524499150042.

The contradiction: In many normal cells, lactate production is typically restricted to anaerobic conditions when oxygen levels are low, however, cancer and embryonic cells preferentially channel glucose towards lactate production even when oxygen is plentiful, a process termed “aerobic glycolysis” or the Warburg Effect [2].

The explanation from the standpoint of human photosynthesis: If the combination of oxygen with glucose was the true source of energy of the eukaryotic cell, we would find that the more you have a tissue metabolic activity, more oxygen consumption and glucose would be the rule, however, cancer cells and the normal embryonic cells whose metabolic and mitogenic index is remarkably high, the cell switches to the use of glucose is very inefficient, although it is an intricately regulated process. Highly proliferative cells need to produce excess lipid, nucleotide, and amino acids for the creation of new biomass. Excess glucose is diverted through the pentose phosphate shunt (PPS) to create nucleotides. Fatty acids are critical for new membrane production and are synthesized from citrate in the cytosol through the action of ATP-citrate lyase (ACL) to generate acetyl-CoA.

Above is consistent with our assertion that glucose is only source of biomass, and not energy, for the latter our body is able to take it from the water through dissociation and back together of water molecule. Do not forget that if the energy source was glucose, diabetics should then be able to climb walls.

Traditional view: The PO_2 of the gaseous oxygen in the alveolus averages 104 mm Hg, whereas the PO_2 of the venous blood entering the pulmonary capillary at its arterial end averages only 40 mm Hg because a large amount of oxygen was removed from this blood as it passed through the peripheral tissues. Therefore, the initial pressure difference that causes oxygen to diffuse into the pulmonary capillary is $104 - 40$, or 64 mm Hg. Pulmonary capillary equilibrates with the alveolar PO_2 in about 0.25 seconds.

The contradiction: To raise blood PO_2 40 to 104 mm Hg are required 0.25 seconds, conversely, to reduce such PO_2 from 104 to 40 mm Hg blood must travel approximately 95,000 km of capillaries. The differences between the values of pH, P_{CO_2} , bicarbonate and PO_2 in venous and arterial blood are reported [3] as follows:

The mean arterial pH value was 7.384 with a SD of 0.124; the mean venous pH was 7.369 with SD 0.12. The mean arterial value of P_{CO_2} was 39 mmHg with SD 15.11, in the venous side, the mean P_{CO_2} value was 42 mmHg with SD 20.71. Bicarbonate arterial value in mEq/l was 23.58 with SD 8.86, and in the venous side was 24.32 mEq/l with SD 9.43. In regards PO_2 the mean arterial value was 115 mmHg with SD 64.5, and in venous side, the mean value was 50 mmHg with SD of 24.39. As expected, venous PO_2 and arterial PO_2 did not show good agreement as pH, P_{CO_2} and bicarbonate values.

By following the laws of simple diffusion, oxygen concentrations in the blood are constantly changing, they tend to go more to the area of lower concentration, and this is in a continuous, relentless, only the presence of other influences in such behavior.

If the PO_2 rises from 40-104 mmHg in 0.25 seconds, why don't it drops below 40-50 mm Hg in venous blood? Since the distance and the time are erythrocytes in the systemic circulation is much greater than the time course that occurs in the lungs.

The explanation from the standpoint of human photosynthesis: Hemoglobin has the ability to irreversibly dissociate in water molecule, as does another molecule that is almost identical to it: chlorophyll. In this way the oxygen that enters the blood and is carried mainly by the Hb not only comes from the pulmonary alveoli but hemoglobin itself.

You might think that the proportion of oxygen corresponding to the dissociation of water by the hemoglobin is at least the equivalent of 40-50 mmHg. Thinking in this way does not have to generate hypotheses complex or confusing.

Also the rest of the values reported in arterial and venous blood are consistent with our finding intrinsic property dissociates the hemoglobin molecule irreversibly water as it makes its twin molecule: chlorophyll.

Namely, the pCO₂ rises much more than it reflects the measurement of the gas in venous blood, as carbonic anhydrase catalyzes reversible and constantly the combination of CO₂ with water. so that their values remain low, within very narrow limits, but as these values are rising as the hemoglobin captures CO₂ as it passes through the rest of the body, although the ability of carbonic anhydrase catalysis approaches the limits of the diffusivity, the relatively high levels of CO₂ begin to affect the ability of hemoglobin to dissociate the water molecule, and this is reflected in the levels of hemoglobin oxygen generated gradually begin to decrease, coupled other known or unknown factors, such as changes in the properties of the water that induces high levels of CO₂ and bicarbonate. And in turn conformational changes in the hemoglobin molecule, as low oxygen levels impoverish the carrying capacity of CO₂.

The pH value goes from 7.384 to 7.369, thereby hydrogen ion concentration increases in the venous side. The mean arterial value of Pco₂ was 39 mmHg with SD 15.11, in the venous side, the mean Pco₂ value was 42 mmHg with SD 20.71; although the dispersion is much, making it difficult to draw conclusions, however it is obvious that as the blood circulates more and more CO₂ will attach to the blood, and not because there is tissue that produce more CO₂ than others, but as the hemoglobin moves through the capillaries of the body, more and more CO₂ is attached. And the frantic action of carbonic anhydrase is reflected in the increase of bicarbonate on the venous side.

2 The Fick Law

The diffusion coefficient of a gas is directly proportional to its solubility and inversely related to the square root of its molecular weight (MW):

$$D = \text{Solubility} / (\text{MW})^{1/2}$$

Therefore, a small molecule or one that is very soluble will diffuse at a fast rate; for example, the diffusion coefficient of carbon dioxide in aqueous solution is about 20 times greater than that of oxygen because of its higher solubility, even though it is a larger molecule than O₂.

The Fick law states:

- That the rate of gas diffusion is inversely related to membrane thickness. Thereby the diffusion of a gas will be halved if membrane thickness is doubled.
- The rate of diffusion is directly proportional to surface area.
- Two lungs that have the same oxygen diffusion gradient and membrane thickness but with different alveolar-capillary surface area, the rate of diffusion will differ in the same proportion. (If one lung has twice the alveolar-capillary surface area, the rate of diffusion will differ by two fold.)

	Inspired Air	Expired Air	Right Heart	Left Heart
O ₂	160 mmHg	116 mmHg	40 mmHg	95 mmHg
CO ₂	0.3 mmHg	32 mmHg	46 mmHg	40 mmHg

According to the above table and according to the differences between the inspired and expired air have to the lung absorbs only a quarter of the available oxygen in the alveoli. And conversely, the CO₂ is increased about 100 times.

If the oxygen had a metabolic function so important to the human body as has been claimed for centuries, it is difficult to accept that their movement through the lung is governed by the laws of simple diffusion. We would be saying that one of the pillars of life, oxygen can be at the mercy of chance? Their levels, which clearly are important, in the lung start randomly?

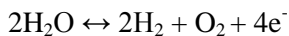
In contrast, CO₂ is transported by hemoglobin, 15 to 25 % of carbon dioxide is carried this way; one hemoglobin molecule can carry 4 oxygen and 4 carbon dioxide molecules at the same time, CO₂ in a different place to oxygen, and 7 % of CO₂ also is transported dissolved in plasma, and 70 % is transported as bicarbonate ions with the essential help of the carbonic anhydrase, an enzyme abundant in erythrocytes, an enzyme whose function to catalyze the reversible combination of CO₂ with water, has a capacity that is approaching the limits of the diffusivity, it reaches a million molecules per second, we generated the following doubt: the combination of CO₂ with water spontaneously happens, but not with the right intensity to be compatible with life, so it is necessary to be catalyzed and at a rate that approaches the limits of the possible, and the enzyme that nature development for this purpose is found in all mammals; what are the reasons for the insistence of nature to ensure that CO₂ levels are kept within well-defined limits?

Certainly the action of the enzyme carbonic anhydrase requires free chemical energy.

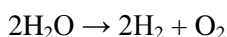
The answers we can give following the philosophical premise that science should be simple is:

- Because oxygen levels are not as important as those of carbon dioxide.
- Oxygen is essential for life, but too much oxygen can be harmful to both cells and the organism.
- The main function of the oxygen in the lungs and blood is to facilitate the transport of CO₂, the allosteric modification that produces the oxygen in the hemoglobin molecule is important in the dynamics of CO₂, is an observed fact that hypercapnia, hypoxia worsens.
- CO₂ levels are tightly regulated, although not necessary for life, as it is a waste cell, the result of metabolism, and oxygen is considered essential for life, enters the lung alveoli to the blood following purely the laws of simple diffusion, but also, only absorbs quarter of that, it seems that we can afford to waste it.
- From the point of view of human photosynthesis or intrinsic property of melanin to dissociate and re-form the water molecule, oxygen is a necessary evil.
- When the water molecule dissociates, it releases diatomic hydrogen and oxygen, but the really valuable is the hydrogen as energy carrier is that more uses nature in the entire universe.
- Oxygen is toxic at any concentration.

Furthermore, the eukaryotic cell has the ability previously unknown to take energy from water, dissociating and re-forming said molecule, so that the body cells are able to produce oxygen for themselves. The hitherto unknown intrinsic property of the melanin from the molecule and re-form it can be represented as follows:



Human photosynthesis name derives from the resemblance to the also first reaction of plant photosynthesis, which begins with the irreversible dissociation of the water molecule.



The photonic energy transduction in free chemical energy inevitably requires dissociation of the water molecule, at least on planet Earth seems to have no choice in nature.

The leaf chlorophyll molecule dissociates irreversibly water, using the ends of visible light: the purple and red. It is efficient only during the day. In the case of humans, melanin has the amazing ability to dissociate and re-form the water molecule, using the entire electromagnetic spectrum, as melanin is able to absorb any type of energy, is the substance for something more known dark, humans thus dissociate and re-form the water molecule both day and night.

2.1 Traditional View

Let us now examine oxygen levels and carbon dioxide in and out of the heart. In the venous blood (right heart) O_2 is 40 mm of mercury and in the arterial blood (left heart) is 95 mm Hg. That is an O_2 difference of 55 mm Hg, and on the side of CO_2 we have that in venous blood (right heart) is 46 mmHg and in arterial blood (left heart) is 40 mm Hg, this is a difference of only 6 mm Hg.

Random is oxygen levels rise from 40 to 95, and decrease of 46-40 CO_2 levels inclusive nature use what is called convergent evolution, as are several known types of carbonic anhydrase, but every one of them has the same goal: catalyze the reversible combination of CO_2 with water. Since the process, when it happens randomly, it is not compatible with life, needs to be catalyzed to occur within the appropriate margins. It seems that nature CO_2 management in the pulmonary alveoli is much more important than oxygen management.

2.3 Contradiction

Respectfully, if the oxygen was important, we would be before a tightly regulated process, which is much more compatible with life than a system that is based on the laws of simple diffusion.

Furthermore under steady-state conditions, approximately 250 ml of oxygen are transferred to the pulmonary circulation per minute (V_{O_2}) while 200 ml of carbon dioxide per minute are removed (V_{CO_2}). The ratio $V_{\text{CO}_2} / V_{\text{O}_2}$ is the respiratory exchange ratio (R) and is 0.8 in this case.

The incognita is: our body needs 250 ml per minute of oxygen to increase from 40 to 95 levels of oxygen, and requires extracting 200 ml of CO_2 per minute to decrease these

levels 46-40? It is not consistent, since CO₂ is not compressed oxygen, the volumes and the mm of mercury of both compounds (O₂ and CO₂) should be more similar, as the other one depends, thereby cannot be disparate. We could think of many hypotheses, but try to make science simple, following the advice of the philosophers.

2.3 The Explanation from the Standpoint of Human Photosynthesis

Pulmonary capillary blood flow has a significant influence on oxygen uptake. Transit time or the time required for the red cells to move through the pulmonary capillary is approximately 0.75 seconds.

During transit time, the alveolar gas tension equilibrates with the gas tension in blood. Cardiac output can change dramatically transit time.

Cardiac output	Blood flow (lung capillary)	Transit time
↑	↑	↓

Gases that diffuse across the alveolar-capillary membrane and dissolves in the blood but do not combine with hemoglobin are perfusion limited, this is: the amount that can be taken up is entirely limited by blood flow, not by diffusion of the gas.

A gas that diffuses across the alveolar-capillary membrane and has strong affinity for hemoglobin is diffusion-limited and not limited by blood flow.

The equilibration curve for oxygen lies between previous examples. Under resting conditions, the capillary Po₂ equilibrates with alveolar Po₂, when the blood has spent about one third of its time in the capillary. Beyond this point there is no additional transfer of oxygen.

This is a key data, beyond this point there is no additional transfer of oxygen. In light of the discovery of human photosynthesis this concept is far from the true nature of the body.

The effect of oxygen coming from the dissociation of water by hemoglobin on the oxygen tension in the blood is not easy to distinguish, but we can infer, for example alveolar oxygen is equilibrated with oxygen from the blood in 0.25 seconds following the laws of diffusion simple, and the manner in which the oxygen presumably moves to and from the tissue is through the same principle: the simple diffusion.

So if the conditions, the event happen: if the concentration of oxygen in the tissues is sufficiently low, say about 40 mm Hg, at 0.25 seconds would pass blood oxygen to the tissues. And digital pulse oximetry measures peripheral blood hemoglobin (SaO₂%) is a reliable tool that sheds light on our hypothesis. Digital pulse oximetry results were defined as abnormal if there was a decrease of more than 2% in saturation at the toe from the finger [4, 5]. The oxygen saturation, expressed as a percent is the simple fraction relating oxygen content and capacity:

$$\% \text{ oxygen saturation} = \text{oxygen content} / \text{oxygen capacity} \times 100$$

Pulse oximetry offers a repetitive, noninvasive measure of systemic oxygen saturation using the distinctive light absorption properties of oxygenated and deoxygenated hemoglobin in pulsating tissue [6].

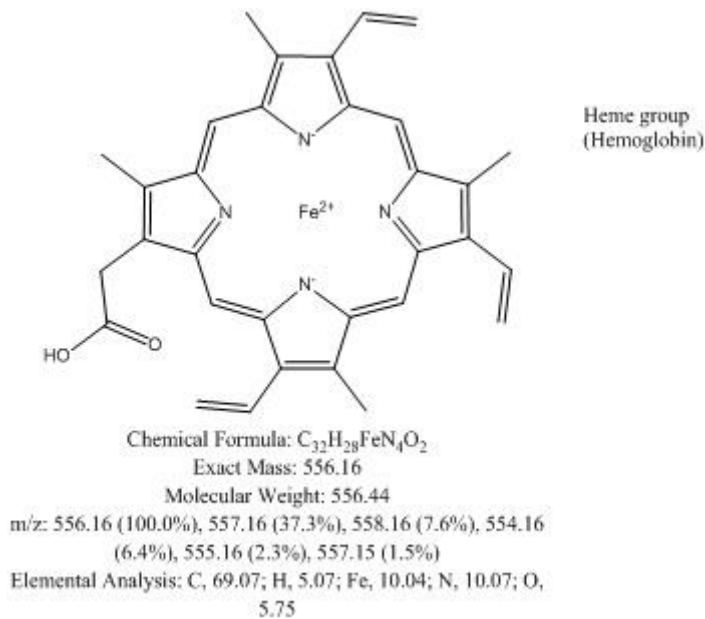
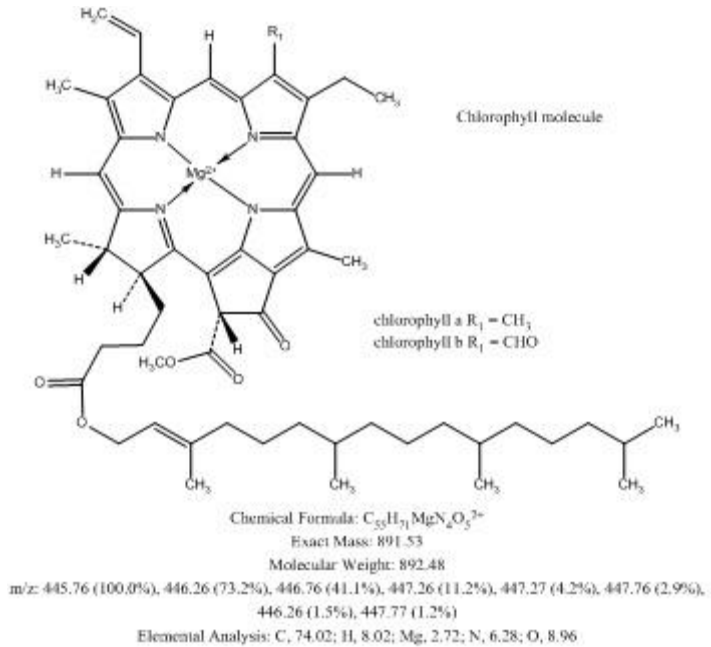
Digital pulse oximetry had a sensitivity of 77 % and specificity of 97 % in the study of lower extremity arterial disease in asymptomatic patients with diabetes mellitus. $\text{SpO}_2 \leq 95\%$ is considered appropriate. In studies of healthy populations, the distribution of SpO_2 measured in the lower extremity at 24 hours of childbirth was reported to be $97.3 \pm 1.3\%$. A mean SpO_2 of 95.4 % at 24 hours of life from a population evaluated at 5300 ft. In general, the mean difference between SpO_2 measurements in the upper and lower extremities is $< 1\%$ [7].

Certainly the distance between the finger and the toe is much larger than the average length of the pulmonary capillaries, absent the generation of oxygen through hemoglobin, SaO_2 should be close to 40 mm Hg in the extremities, since the distance to the heart of them is sufficient for oxygen concentration was significantly decreasing, and contradictorily remains at levels close to 95%, as if within the lung itself or the immediate, which contradicts the theory that only oxygen enters the blood through the pulmonary alveoli and on the other hand supports our finding that hemoglobin dissociates the water molecule, which explains in turn, the energy source of the erythrocyte, as this does not have mitochondria.

Recall that when water molecule is cleaved, the photon energy is transformed into free chemical energy, which is transported by the molecular hydrogen, which, in turn, is not combined with water. In the case of hemoglobin, color allows us to think that is absorbing visible electromagnetic radiation mainly close to purple, as this reflecting the waves near the red, say between 650 and 700 nanometers, therefore our senses perceive erythrocytes red.

On the other hand, if we try to explain why no oxygen saturation declines in peripheral circulation based on the traditional dogmas, we have to implement increasingly complex theories, however, if even for a moment put into the equation the property intrinsic of hemoglobin to dissociate the water molecule, things change, because if the erythrocyte is producing oxygen continuously, then O_2 levels do not decrease until the CO_2 increases, since the carbon dioxide decreases oxygen levels at least two reasons: causes an allosteric change in the hemoglobin molecule which decreases its affinity for O_2 and also its efficiency to dissociate the water molecule. The properties of water are also changed by higher concentrations of the CO_2 molecule.

The hemoglobin and chlorophyll molecule is almost identical (see below), therefore it is perfectly possible that both molecules possess the ability to dissociate the water molecule irreversibly. Like chlorophyll, which expellee oxygen to the atmosphere, hemoglobin expels oxygen to their immediate environment, and part of it is taken up by the prosthetic group of hemoglobin: iron.



Oxygen-carrying capacity of whole blood is 16-25 ml O_2 /dl, 20.1 ml O_2 /dl in average. Thereby there are 10,000 ml of oxygen in the blood at a given moment.

15 g Hb/dl x 1.34 ml oxygen/g Hb= 20.1 ml O_2 /dl

Under steady-state conditions, approximately 250 ml of oxygen are transferred to the pulmonary circulation per minute (V_{O_2}) therefore to replenish 10 liters of oxygen, we

require 40 minutes. Since only absorb a quarter of the available oxygen in the alveoli (from 160 to 116 mm Hg of O₂) to absorb all of the oxygen, would suffice to keep him longer, breathing rate required would be less. Instead of 12 to 18 per minute, may be 4 or 5 per minute. But that would not be compatible with CO₂ levels we require to live.

Thus when analyzing the biodynamic O₂ and CO₂ have to take into account that this, oxygen, occurs in the erythrocyte by hemoglobin and in cells of the economy by melanin, so the role of inspired oxygen is actually secondary. The metabolite that we bring to the forefront is the CO₂ because very fast alter the biochemistry of life, and if the concentrations are high enough, can cause death in about 30 seconds.

3 Fetal Breathing Movements

Intermittent breathing activity is a normal feature of fetal life with a tendency to be stimulated by carbon dioxide and inhibited by hypoxia [8]. Fetal breathing is defined as the contraction of the diaphragm resulting in downward and outward displacement of the abdominal contents and inward displacement of thorax. No breathing at all observed before 26 weeks' gestations, fetal hiccups being the predominant type of diaphragmatic movement until 26 weeks' gestation.

It seems that the fetus does not require breathing, we could argue that the fetus needs oxygen comes through the umbilical artery, although this will require O₂ saturation close to 100%, and ironically it is not, as is usual concentration less than 50%. So the questions that emerge from clinical observations are: Why is the fetus does not breathe? Where does the oxygen necessary?

And as happens childbirth, respiratory rate changes dramatically, because in the first year of life has a frequency of 30-60 breaths per minute. So for almost no breathing, suddenly the need to breathe becomes frantic as it is in the order of 30-60 breaths per minute.

3.1 The Explanation from the Standpoint of Human Photosynthesis

In light of the discovery of human photosynthesis revolves around the response to CO₂, since the cells of the body can produce its own oxygen. Water can dissolve thousands of times more CO₂ than air, so the amniotic fluid with carbon dioxide form bicarbonate, and does so very quickly thanks to an enzyme called carbonic anhydrase. Thus the fetus has no need to breathe inside the uterus. After birth, the CO₂ be ejected into the atmosphere, so the respiratory rate rises abruptly to 30-60 breaths per minute during the first year. This change in respiratory rate is needed to compensate the rate at which CO₂ is diluted in the air. Let us return to the patterns of photosynthesis in plants and humans.

According to the above schemes, we can say that photosynthesis teaches us that the food, the body makes skin, nails, hair, bone, muscle, neurons, genes, etc.; but the energy, that nobody knows what it is, no one has seen, do not know if it's a circle, a line, a wave, a notch, etc., energy is defined as anything that produces a change, and metabolism means change. Then, our body takes the food carbon chains of different lengths and branches forming bio-molecules, but the energy is taken from water.

And the same thing happens the fetus, from the mom-blood takes the building blocks with which it forms the biomass, but the energy is taken from the amniotic fluid is 99% water. And it is obvious, as when the fetus brings much water is bad (polyhydramnios), and when he brings little too (oligohydramnios), because the amount of water is accurate.

So oxygen is not required to bring the outside and each as all of the body's cells have melanin and therefore possess the ability to split water to produce hydrogen and oxygen at their own. Thus low concentrations of oxygen in the umbilical artery stop being contradictory, because the amount of oxygen that goes from the uterine arteries to the umbilical artery is governed by the laws of simple diffusion, not forgetting that fetal hemoglobin also has the intrinsic property of irreversibly dissociate water molecule.

The affinity of hemoglobin for CO is 250 times that for oxygen, thereby blood circulation is primarily intended to remove CO₂, and transport of the building blocks of biomass. Therefore, the fetus does not require breathing, as water has a great ability to dissolve CO₂, thousands of times more than air, even if it requires carbonic anhydrase, which is present from the early stages of gestation, and therefore, as happens childbirth and formed alveolar air interface, then the respiratory rate changes, because then if required at a high level in order to remove CO₂.

3.2 Traditional View

As the first step in the oxygen-transport chain, the lung has a critical task: optimizing the exchange of respiratory gases to maintain delivery of oxygen and the elimination of carbon dioxide [9]. A fact that shows the complex hypothesis we have had to implement trying to argue that the source of oxygen in the blood is entirely through the pulmonary alveoli is despite more than two decades of research, the mechanisms of pulmonary gas exchange limitations during exercise are still debated [10]. In healthy subjects, gas exchange, as evaluated by the alveolar-to-arterial PO₂ difference (A-aDO₂) worsens with incremental exercise. The hypercapnia has a marked vasoconstrictor effect, since physiological levels of CO₂ stimulate photosynthesis in human; which is consistent with the old observation that the best vasoconstrictor is high levels of oxygen; and oppositely

hypocapnia induces significant vasodilatation in lung. It is difficult to study the effects of hypocapnia in pulmonary circulation because of its low initial tone; attempts to vasodilate the normal pulmonary circulation are bound to fail [11].

It is difficult to understand data as follows: resting muscle oxygen consumption (rmVO_2) was higher in Multiple Sclerosis compared to Healthy Controls [12]. Well since the dogma indicates that the energy of the cell is obtained by combining oxygen with glucose, theoretically the muscles of a patient with multiple sclerosis should consume less oxygen and glucose because they are sick.

In the so called oxygen diffusion limitation, gas exchange abnormalities primarily reflect a widespread non-uniform dilatation of pulmonary vasculature at both the pre-capillary and capillary levels [13]. The picture is very complicated.

3.3 The Explanation from the Standpoint of Human Photosynthesis

Free chemical energy that is generated by the intrinsic property of hemoglobin to dissociate the water molecule irreversibly spreads following the laws of simple diffusion, i.e. tends to occupy all the space around him [14]. The erythrocyte cell is not to spend much energy as nucleated cells therefore likely free chemical energy generated also reach the immediate environment of the erythrocyte, i.e. plasma albumin.

The function of circulating albumin in critical illness is not fully understood [15], it may differ significantly from that in healthy subjects. A low serum albumin concentration in critical illness is associated with poor outcome. Despite theoretical advantages for using human albumin solution as a plasma substitute, studies have shown that correcting hypoalbuminaemia has no impact on outcome in the critically ill.

In humans, albumin is the most abundant plasma protein, accounting for 55-60 % of the measured serum protein. It is a single polypeptide chain of 585 amino acids with a 66 500 Da of molecular weight. The chain has not carbohydrate moiety and an abundance of charge residues, such as lysine, arginine, glutamic acid and aspartic acid.

Albumin is a very flexible molecule, changing shapes readily with variations in environmental conditions and with binding of ligand. The structure of albumin is considered resilient owing to disulphide bridges. Albumin will regain shape easily, but retain and regain the form in the case of any compound requires free chemical energy.

The normal trans-capillary escape rate for albumin increases up to 300 % in patients with septic shock, and by 100 % after cardiac surgery. The rate of albumin synthesis may be significant altered in the critically ill. A sustained inflammatory response in critical illness may lead to prolonged inhibition of albumin synthesis.

The structure of the albumin molecule is such that it can incorporate many different substances. Most strongly bound are medium-size hydrophobic organic anions, including long chain fatty acids, bilirubin and haematin. Albumin has a strong negative charge, but there is little correlation between the charge of the compound and the degree of binding to albumin. Albumin binding capacity decreases with age. The total body albumin pool measures about 3.5-5.0 g kg^{-1} body weight (250-300 g for a healthy 70 kg adult). The normal range is 3.4 - 5.4 grams per deciliter (g/dL). The plasma compartment holds about 42 % of this pool, the rest being in extravascular compartments. Each 24 hours, 120-145 g of albumin is lost into the extravascular space. Most is recovered back into the circulation by lymphatic drainage. Albumin lost into the intestinal tract (1 g each 24 hours) is digested releasing amino acids and peptides which are reabsorbed. Of the about 70 kg of

albumin that passes through the kidneys every 24 hours, only few grams pass through the glomerular membrane. Urinary loss of albumin is usually no more than 10-20 mg day⁻¹.

Albumin must cross capillaries. Most organs in the body have continuous capillaries, but in some there are wide-open sinusoids (liver, bone marrow) or fenestrated capillaries (choroidal layer, choroidal plexus, small intestine, pancreas adrenal gland). Half of the escaping albumin does so through the continuous capillaries, and there appears to be an active transport (energy is required) to facilitate this. Albumin binds to albumin, a surface receptor, which is widely distributed in many capillaries, except in the brain. Bound albumin enters vesicles within the endothelial cell and is discharged on the interstitial side within 15 seconds; thereby the process requires intracellular free chemical energy constantly. The rate of transfer is increased with the addition of long-chain fatty acids to albumin, and with the cationization (H₂⁺) and glycosylation of the albumin molecule. All processes require free chemical energy to be made.

Albumin synthesis in humans takes place only in the liver. Albumin is not stored but is secreted into the portal circulation as soon as it is manufactured, about 12-25 g of albumin per day. The synthetic pathway is common to eukaryotes and is also used for synthesis of other proteins.

Theoretically, the abundance of sulphhydryl (-SH) groups on the albumin molecule is favored by the molecular hydrogen is released by irreversible dissociation of the water molecule by hemoglobin. It is probably that albumin binding capacity is increased with the human photosynthesis enhancement.

The binding of compounds with albumin as well as the conservation of the newly formed bond and subsequent release of the same in a strictly regulated way that is compatible with life, i.e. not dependent on chance, requires the constant presence of free chemical energy in the surrounding.

There biochemical processes that take place in the bloodstream, such as critical parts of cholesterol metabolism, also require free chemical energy. Thereby white blood cells that indeed require more energy than red blood cells instead contain melanin.

Pathways of intracellular oxygen movement

From a mechanistic standpoint, there are essentially two major routes for the intracellular movement of oxygen in mammal cells:

- Physical solution in the solvent systems of the cell
- Bound as a dissociatable ligand to an oxygen-carrying macromolecule.
- Transcellular movement of oxygen from capillaries to mitochondria via either of these pathways occurs by molecular diffusion
- Thereby can be affected by cellular temperature and solubility of gases.

Constraints in the movement of oxygen are most pronounced at the cold body temperatures; however the polar seas of the globe support abundant and successful population of fishes and invertebrates.

Changing temperature affects both the solubility and diffusion coefficient (Do₂). Do₂ in water increases by approximately 3 % for each rise in temperature of 1°C. By other side, the solubility of oxygen decreases with increasing temperature.

The reduction of Do₂ in the aqueous cytoplasm of cells with decreasing temperature is attributable to two factors: a reduction in the kinetic energy of the system and an increase in cytoplasmic viscosity which is inversely related to cell temperature.

The effect of temperature on the viscosity of aqueous solutions is considerable. Between 25 and 5 °C, the viscosity of pure water increases by more than 70 %: from 0.89 to 1.52

cP. Thus diffusion of oxygen dissolved in the aqueous compartment of the cell appears to be quite sensitive to decreasing temperature.

The considerations above described indicate that both major routes of intracellular oxygen movement: oxygen in physical solution and bound to Hb, should be severely compromised at cold body temperature. The simplest solution, lowering of cytoplasmic viscosity, is not an available option because the intrinsic properties of water.

Thermal acclimation of fishes was capable of inducing important changes in subcellular anatomy. During acclimation of crucian carp from 28 to 2 °C, the mitochondrial density of red muscle fibers increased by 80 % [16].

The very high mitochondrial volume densities observed in oxidative muscles of Antarctic fishes, more than 35 % of cell volume, thereby high mitochondrial populations were an important requirement for aerobic muscle function at cold temperature. But these mitochondria populations in cold-adapted animals are often so densely clustered that it is difficult to envision how oxygen might pass to those organelles deep within the cluster.

Have been observed also an increase in the content of intracellular neutral lipid droplets. The percentage of muscle cell volume that is displaced neutral lipids droplets increases from 0.6 to 7.9 % between acclimation temperatures of 25 and 5°C.

It is hard to belief that oxygen is transported from blood to mitochondria along channels of high solubility within the cell.

4 Conclusions

Carbon dioxide is produced by cell metabolism in the mitochondria. The amount produced depends on the rate of metabolism and the relative amounts of carbohydrate, fat and protein metabolized. The amount is about 200 ml min⁻¹ at rest and eating a mixed diet. This utilizes 80 % of oxygen consumed, giving a respiratory quotient of 0.8, which is calculated as follows:

Respiratory quotient = rate of carbon dioxide production / rate of oxygen consumption

It has been calculated that our body, at rest, requires: 3.5 ml of oxygen per kilogram of body mass per minute. So a 70 kg man, at rest, requires 245 ml of oxygen per minute. Under steady-state conditions, approximately 250 ml of oxygen are transferred to the pulmonary circulation per minute (V_{O_2}). This is contradictory, because it would be tantamount to saying that at rest the amount of oxygen that passes from the lungs into the blood just enough, when we know that the body always has a large reserve of compounds that can be required for walking, running, etc.

The total body content of carbon dioxide including bicarbonate ion is 120 liters or 100 times that of oxygen [17]. Carbon dioxide is 20 times more soluble than oxygen.

Considering the intrinsic property of melanin to dissociate and re-form the water molecule, which means that every cell in our body is capable of generating oxygen by itself, and the above coupled intrinsic property of hemoglobin irreversibly dissociate the water molecule, then the oxygen that passes from the atmosphere to the lungs and from there to the blood stops have seemed enormous importance, because according to the above one is a complement of the total.

An example of the meta-analysis we have more studies that have been carried out on oxygen consumption in the brain, where values derived from tissue spectrophotometry indicate that brain tissue P_{O_2} values may be considerably lower than 20 mm Hg [18]. It is now well documented that most hydrophilic molecules and ion pass through the blood-

brain barrier extremely slowly. The permeabilities to small solutes have been found to be $\approx 1/100$ those found for the capillary membrane in muscle tissue.

In isolated mitochondria, cytochrome aa3 is completely oxidized above P_{O_2} values of 1.0 mm Hg. Reflectance spectrophotometry reveals a significant amount of reduced cytochrome aa3 in the brain of anesthetized animal suggesting that very low P_{O_2} values may be present in tissue.

Neither value is explainable with the classical Krogh model, which envisages no resistance to the passage of oxygen from blood capillary to tissue. Confocal microscopy of rat brain cortex indicates that 10 to 20 % of cerebral capillaries may not contain erythrocytes at any given moment. Analysis indicates that the transfers of both $[^{18}O] O_2$ and $[^3H]$ water indicators from blood to brain are barrier-limited with the former highly so because of large red blood cell capacity for oxygen, and the proportion of the tracer oxygen returning to the circulation from tissue is a small fraction of the total tracer emerging at the outflow.

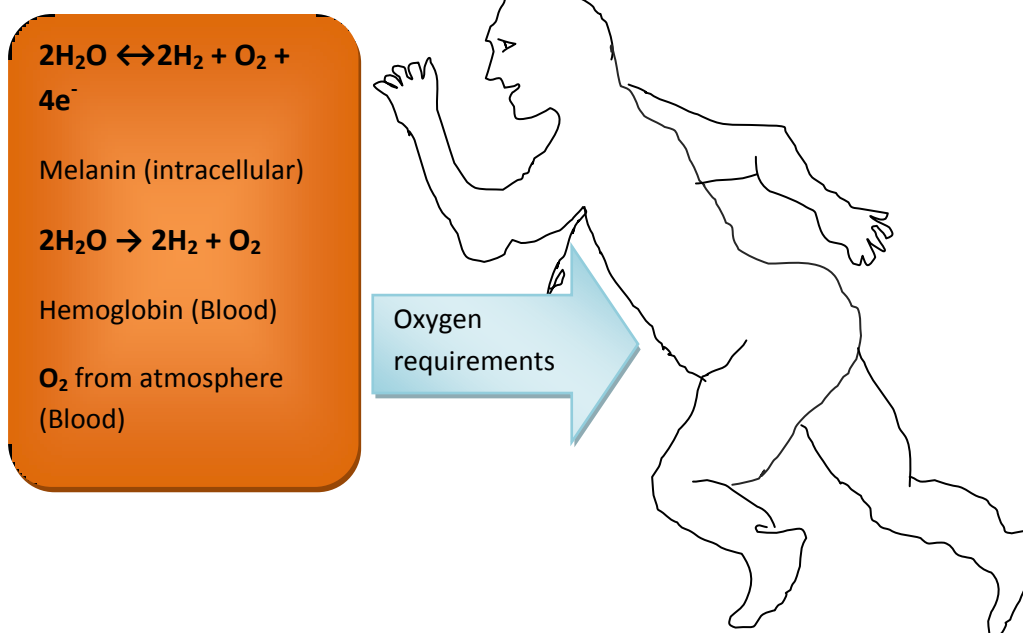
Our finding in the human retina initially and then the rest of the body of important and previously unknown role of melanin as photonic energy transducer in free chemical energy are consistent with the findings that hardly pass oxygen blood-brain barrier. For one oxygen needs are covered by the dissociation of the water molecule, and energy needs are largely solved by molecular hydrogen, which when not combined with water can reach the remotest area of the cell, it follows the laws of simple diffusion, conducting at least two important functions: delivery of energy and also as an antioxidant, since hydrogen is the best.

The significant amount of reduced cytochrome aa3 can be explained in large part by the hydrogen generated from the dissociation of the water molecule.

From Camillo Golgi, in 1886, it was said that should astrocytes play an important role in the distribution of energy substrates from the circulation and neurons. It is a well established fact that neurons contribute at most 50 % of cerebral cortical volume. An astrocyte:neuron ratio of 10:1 is a feature of most brain regions.

Synaptically released glutamate triggers glucose use in astrocytes, but not as a source of energy but only source of biomass, for example to replenish the neurotransmitter pool of glutamate. Glutamate stimulates the glucolytic processing of glucose in astrocytes, as indicated by the increase in lactate release. Thereby glutamate stimulates aerobic glycolysis (i.e. the transformation of glucose into lactate in the presence of sufficient oxygen) in astrocytes. In vitro lactate can adequately maintain synaptic activity, but in vivo, lactate is not an adequate substrate since it crosses only marginally the blood-brain barrier [19]. Other contradictory finding is that cerebral blood flow and glucose use are not always coupled.

Figure 1 Oxygen requirements of the human body



Levels of intracellular oxygen requirements are fully covered by melanin through dissociation and subsequent re-formed from the water molecule. In blood, the oxygen required is filled by the gas exchange in the lungs and through water dissociation that performs hemoglobin. Maybe the values in blood are close to 50/50, but the continuous production of oxygen by hemoglobin allows the levels do not decrease to less than 40 mmHg in any part of the body, while gas exchange at the level of pulmonary alveoli, which is somewhat sharp in the lungs, allowing mainly the CO_2 is expelled into the atmosphere. The administration of exogenous carbonic anhydrase reduces post exercise hypercapnia without changing oxygen concentrations [20]. Which actually supports the management of CO_2 is the main purpose of blood circulation, rather than maintaining oxygen levels; since the cell is independent of oxygen from the outside, as it occurs on its own, the blood has hemoglobin, which possess the ability to dissociate the water molecule also produces oxygen, so oxygen from the atmosphere only part of the equation, but it is not only or main variable that had been considered to date.

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