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Review

Energy metabolism during physical exercise: Towards a current conceptualization in physical activity and sport sciences

Jorge L. Petro[1,2,*], Diego A. Forero[3], Diego A. Bonilla[1,2,4,*]

[1] Research Division, Dynamical Business & Science Society—DBSS International SAS, Bogotá 110311, Colombia
[2] Research Group in Physical Activity, Sports and Health Sciences (GICAFS), Universidad de Córdoba, Monteria 230002, Colombia
[3] School of Health and Sport Sciences, Fundación Universitaria del Área Andina, Bogotá 111221, Colombia
[4] Department of Genetics, Physical Anthropology and Animal Physiology, University of the Basque Country (UPV/EHU), 48940 Leioa, Spain
*** Corresponding authors:** Jorge L. Petro, jlpetros@dbss.pro; Diego A. Bonilla, dabonilla@dbss.pro

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Abstract: Energy metabolism is a central topic in physical activity and sports sciences. However, some concepts still require biological contextualization and more precise terminology in scientific literature. In this regard, the purpose of this review was to highlight certain concepts that deserve to be reconsidered and possibly excluded from the vocabulary of exercise and sports sciences. It is argued that the terms “anaerobic” and “aerobic”, used to classify exercises or sports activities, are incorrect and imprecise. Similarly, the persistent use of the term “lactic acid” (i.e., the interchangeable use of lactate and lactic acid, often incorrectly considered the same) consequently leads to the misrepresentation of the phenomenon of “lactic acidosis”, which lacks rigorous biochemical support. Therefore, a conceptual reframing is needed to align with recent findings in exercise biochemistry and molecular biology. The following issues are addressed: i) The estimation of energy system contributions during physical exercise, with emphasis on the most commonly used methods in humans; ii) the classification of energy metabolism—and by extension, exercises—into “anaerobic” and “aerobic”, challenging this dichotomy and proposing a more precise classification into oxygen-independent energy systems (phosphagen and glycolytic) and oxygen-dependent energy systems (mitochondrial oxidative system); iii) the concepts of lactic acid production and lactic acidosis, refuting the idea that lactate accumulation results from oxygen deprivation and highlighting its role as an important metabolic intermediate; and iv) the interaction and contribution of energy systems during physical exertion, stating that energy systems are not activated sequentially but simultaneously, with their predominance depending on metabolic demands. By aligning terminology with contemporary findings in biochemistry and molecular biology, this perspective enhances the understanding and critical analysis of metabolic concepts in sports science education and professional practice, encouraging their adoption based on scientific evidence.

Keywords: lactate; energy metabolism; physiological adaptation; metabolic networks and pathways; allostasis

1. Introduction

The study of energy metabolism has been central to both exercise and sports sciences [1]. From optimizing high-performance athletic training to enhancing fitness and health, a comprehensive understanding of the fundamental principles of cellular energy processes is central to the design of effective exercise and nutritional interventions [2,3].

Recent technological advances, and an increased number of research studies in exercise sciences (such as Biochemistry, Physiology, and Molecular Biology of

Exercise) have substantially enhanced our understanding of the complexity of metabolic processes in muscle fibers and their responses to changing energy demands during exercise [4,5]. However, outdated concepts persist in both social media and academic contexts that inaccurately reflect the metabolic functioning of muscle tissue under physiological conditions [6,7]. Such misconceptions need critical scrutiny, in order to have an updated and evidence-based perspective in the field.

This review article aims to re-evaluate and, when necessary, question concepts from the exercise and sports sciences terminology that, according to the latest scientific evidence, should either be revised or reconsidered. The topics discussed in this article are the following: The methods for the estimation of the contributions of energy systems during physical exercise; the classification of energy metabolism and exercises as "anaerobic" or "aerobic"; the interpretation of lactic acid production and the concept of lactic acidosis; the interaction and contribution of energy systems in physical activity, including misinterpretations that have led to conceptual errors.

2. An overview of the methods for the estimation of the contributions of energy systems during physical exercise

A better understanding of the techniques and principles that are used in evaluating the relative contributions of energy systems to human exercise, considering their scope and limitations, is of great interest in sports sciences. This knowledge enhances the conceptual framework and also avoids the misinterpretation and over-simplification commonly encountered when describing the contributions of the energy systems during various types of physical efforts across different intensities. Although a comprehensive review of the technical principles behind each methodology is beyond the scope of this article, we highlight key aspects for their importance and relevance to the study of energy systems.

Throughout history, seminal studies focused on the relative contribution of the energy systems or substrate utilization during a given physical effort, being one of the central areas in exercise physiology [8,9]. Several techniques have been developed to estimate this contribution, considering the intensity and duration of physical exercise. These include oxygen consumption analysis (oxygen uptake, $\dot{V}O_2$), blood lactate concentration, phosphorus-31 magnetic resonance spectroscopy (^{31}P-MRS), and muscle biopsies [9,10]. Even though each methodology has provided valuable insights, this information should be interpreted with caution due to the inherent limitations of each technique. In fact, integrating these methodologies to understand the dynamic interaction of energy systems remains a challenge.

One method to highlight is the 3-component model of energy distribution, also known as Phosphocreatine-Lactate-Oxygen (PCr-LA-O_2), which is widely used due to its validity, cost, and practicality [11]. The PCr-LA-O_2 allows estimating the energy contribution of the phosphagen and glycolysis pathways (extra-mitochondrial) as well as the mitochondrial oxidative system [12,13]. The method integrates key information on phosphocreatine (PCr) resynthesis, lactate production, and $\dot{V}O_2$, providing a comprehensive approach to analyzing the contribution of energy systems during exercise in humans [12,14]. To estimate the energy produced

by each system in the body, it is assumed that one liter of oxygen consumed generates 20.9 kilojoules (kJ) of energy (1 L O_2 = 20.9 kJ). The energy derived from the phosphagen system (E_{PCr}) is calculated using the parameters of the fast component of the Excess Post-exercise Oxygen Consumption (EPOC), which is modeled through a bi-exponential function (Equation (1)) [12]. The equations are described as follows:

$$\dot{V}O_{2(t)} = \dot{V}O_{2baseline} + Af\left[e^{-(t-td)/\tau_f}\right] + A_S\left[e^{-(t-td)/\tau_s}\right] \quad (1)$$

where $\dot{V}O_{2(t)}$ represents the oxygen uptake at time *t*; $\dot{V}O_{2baseline}$ is the oxygen uptake at rest; *A* denotes the amplitude; *td* is the time delay; τ is the time constant, and *f* and *s* indicate the fast and slow components of EPOC, respectively.

To estimate the energetic contribution of the phosphagen system [12], E_{PCr} was calculated as the product of the amplitude (A_f) and the time constant (τ_f) of the fast component (Equation (2)):

$$E_{PCr}(kJ) = A_f \cdot \tau_f \quad (2)$$

The contribution of the glycolytic system (E_{Gly}) is evaluated based on blood lactate concentration, calculated using Equation (3) [12,15]:

$$E_{Gly}(kJ) = \Delta Lactate \cdot 3mL\ O_2 \cdot kg^{-1} \quad (3)$$

where $\Delta Lactate$ represents the change in blood lactate concentration, measured in mmol·L^{-1}, and is calculated as the difference between the maximum concentration and the resting baseline concentration. For this estimation, three milliliters of oxygen are assumed to be equivalent to each millimole of lactate produced, representing the estimated oxygen consumption per kilogram of body mass.

Finally, the energy generated by the mitochondrial energy system (E_{Mit}) is calculated by subtracting resting $\dot{V}O_2$, (measured over 5 min) from maximal exercise $\dot{V}O_2$, using the trapezoidal method [12,15]. Total energy expenditure (E_{TOT}) is then determined as the sum of the contributions from all three systems, as shown in Equation (4) [12]:

$$E_{TOT}(kJ) = E_{PCr} + E_{Glyc} + E_{Mit} \quad (4)$$

The PCr-LA-O_2 method constitutes a valid and reliable approach for evaluating the contributions of energy systems, particularly during high-intensity exercise and intermittent exercise [12,16]. However, it has limitations considering that the parameters employed, such as $\dot{V}O_2$, lactate accumulation, and EPOC, are indirect measures subject to variability [17], which may compromise the accuracy of interpreting metabolic processes at the cellular level. Moreover, in elite athletes, parameters like $\dot{V}O_2$ and blood lactate levels often stabilize, making it difficult to use this method for monitoring energy adaptations in response to training load [12].

On the other hand, it is important to highlight that the recent emphasis on using muscle biopsies/microbiopsy as a research tool has provided valuable insights into energy systems [18,19]. When combined with biochemical, molecular, and cellular analysis techniques, this approach allows for the measurement of substrates (e.g., phosphocreatine, glycogen, and lactate), key metabolic enzymes (e.g., creatine

kinase and citrate synthase), gene expression, and signaling pathways that regulate metabolism (e.g., AMP-activated protein kinase [AMPK]—Peroxisome proliferator-activated receptor gamma coactivator 1-alpha [PGC1-alpha]), as well as other relevant parameters such as intramuscular pH, mitochondrial density, and muscle fiber phenotype changes [19–21]. This method offers a molecular and cellular-level perspective on metabolic activity, enhancing the understanding of energy dynamics during exercise. However, muscle biopsies have limitations, including their invasive nature, which can pose challenges for participants, particularly when multiple samples are required, as well as the costs associated with the techniques used for sample analysis [19].

In view of these challenges, near-infrared spectroscopy (NIRS) has emerged as a promising non-invasive alternative to assess energy metabolism in exercise and sport. This technique allows researchers to measure muscle oxygenation and oxygen consumption in real time, providing valuable information on oxidative metabolism directly at the tissue level [22]. Unlike magnetic resonance spectroscopy, considered the gold standard for assessing bioenergetics, NIRS stands out for being portable, cost-effective, and adaptable to both laboratory and field settings [23]. These features make it particularly useful for studying metabolic adaptations during functional movements or in populations where invasive methods may not be feasible; however, NIRS has its limitations, such as the influence of adipose tissue and the difficulty in distinguishing between hemoglobin and myoglobin signals. Fortunately, advances in technology and correction algorithms have addressed these issues, making NIRS an increasingly reliable tool in metabolic research [23].

In general, integrating these complementary techniques presents a valuable opportunity to achieve a more comprehensive and multi-scale understanding of energy systems during exercise, bridging the gap between cellular and systemic perspectives in this context.

3. The incorrect classification of energy metabolism or exercises as “anaerobic” or “aerobic”

As we elaborate in the following lines, research on this topic has shown that true “anaerobiosis” does not occur during intense physical efforts and, therefore, is not responsible for the increased lactate formation observed during these activities. Studies conducted in the 1980s on animal muscles [24] and later by Richardson et al. [25] on human muscles established that lactate production during physical exertion is not linked to intracellular hypoxia levels.

Notably, it has been reported that during intense muscular activity, intracellular oxygen partial pressure (pO_2) can drop to levels as low as ~3 mm Hg, which is still sufficient to maintain mitochondrial function [26]. In this study, conducted on trained human subjects and using magnetic resonance spectroscopy to measure myoglobin desaturation, it was observed that even under conditions of maximal physical effort, a true state of “anaerobiosis” is not reached, as lactate production is not exclusively associated with cellular hypoxia but rather with other metabolic factors, such as increased anaerobic [sic] glycolysis. This finding suggests that a true state of “anaerobiosis” does not occur during intense physical efforts. This

observation aligns with studies conducted on isolated mitochondria and cellular models (e.g., 32D cells, a murine hematopoietic progenitor cell line commonly used in research) that have evaluated using high-resolution respirometry (Oroboros Oxygraph-2k system) [27]. For instance, at intracellular pO_2 levels below 15 mm Hg under normoxia, mitochondrial respiration is limited by less than 2% due to the high affinity of mitochondria for oxygen (p_{50} typically ranging from 0.01 to 0.10 kPa) [27]. These findings suggest that, under these experimental conditions, oxygen availability is sufficient to sustain mitochondrial ATP production, which could be consistent with the absence of significant oxygen limitations in demanding conditions, such as physical exercise.

In the context of energy metabolism and physical activity, the term "anaerobic" has been incorrectly used (i.e., anaerobic [sic] exercise) to refer to strength, power, or high-intensity activities, often misinterpreting it as synonymous with the absence of oxygen during such efforts [6]. Similarly, the term "aerobic" appears to be misinterpreted as excluding any contribution from "anaerobic" processes (i.e., glycolysis). It is important to clarify that "anaerobic" metabolism does not indicate a pathway that operates without oxygen, but rather one that is independent of oxygen use [6,7]. We align with this updated perspective and encourage the scholar community to classify the two oxygen-independent metabolic mechanisms for ATP restoration as "extra-mitochondrial or oxygen-independent energy systems", encompassing both the phosphagen and glycolytic pathways.

On the other hand, it is also important to reconsider the use of the term "alactic" when referring to the phosphagen system. While it is true that this system does not produce lactate, it is essential to recognize that lactate is continually generated regardless of the state of physical activity or rest, as glycolysis never fully "switches off" [28]. This mischaracterization has led to the inaccurate labeling of explosive exercises (i.e., short duration, high-intensity efforts) as "alactic". Similarly, the glycolytic system should not be referred to as the "anaerobic lactic system", given the misconceptions surrounding the term "anaerobic". Even the traditional distinction between "aerobic" and "anaerobic" glycolysis is conceptually flawed. Glycolysis is a continuous process operating at varying rates regardless of oxygen availability, further highlighting the misconceptions surrounding energy systems [29].

For the aerobic system, it is proposed to use the term Mitochondrial Oxidative System to describe the pathway responsible for the largest contribution to ATP production (or resynthesis) through oxidative phosphorylation. **Figure 1** presents our recommended classification of energy systems based on the available evidence [6,30].

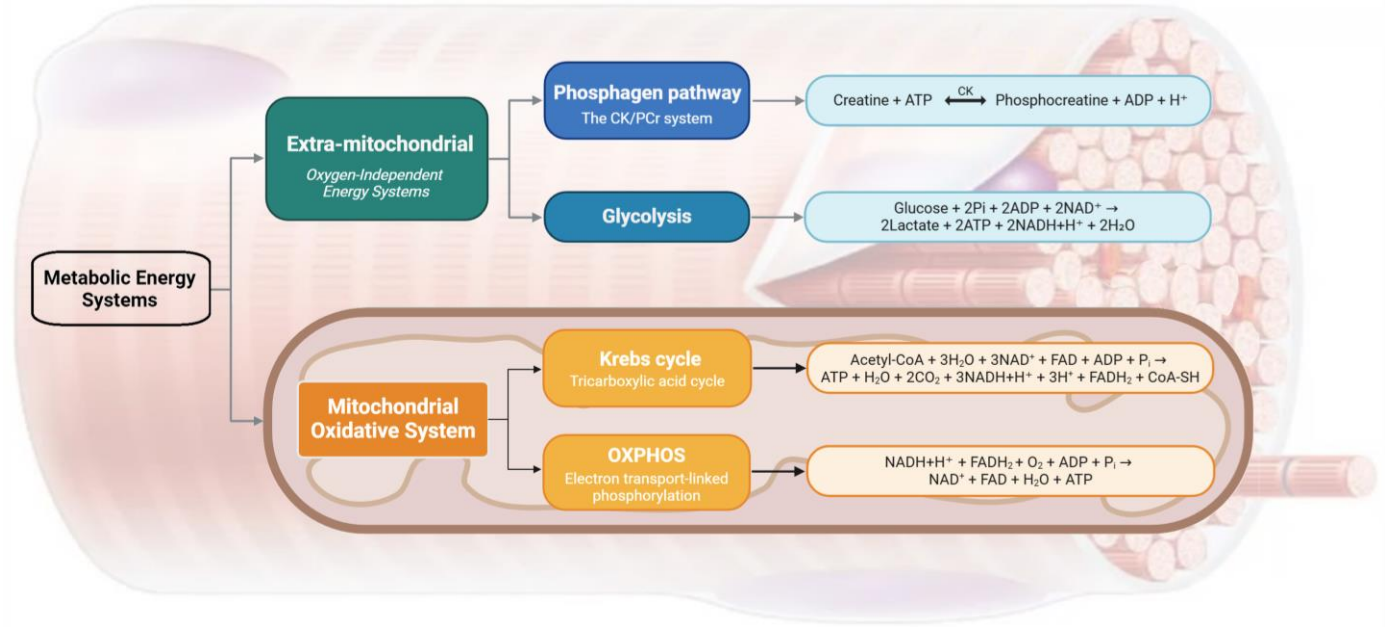

Figure 1. Classification of energy systems. Creatine is converted to phosphocreatine by means of the creatine kinase, which catalyzes the reversible transference of a phosphoryl group (PO_3^{2-}), not a phosphate (PO_4^{3-}), from ATP [31]. Readers should note that the mitochondrial oxidative system is described in general terms, as molecules derived from carbohydrate, fat, or protein metabolism can integrate into either acetyl-CoA or Krebs cycle intermediates. CK: Creatine kinase, OXPHOS: Oxidative phosphorylation, Pi: Inorganic phosphate, PCr: Phosphocreatine.

Source: Created by the authors (D.A.B. and J.L.P.) with BioRender—https://biorender.com/ (accessed on 20 December 2024).

4. The concept of lactic acid production and lactic acidosis

Lactate has undoubtedly been one of the most extensively studied biochemical markers since its discovery [32]. Over the years, shifts in perspective have emerged regarding its role as an energy substrate and its intercellular and intracellular transport, and its function as a signaling molecule, even being recognized as both a myokine and an exerkine [28,33]. Furthermore, it has been positively correlated with the state of metabolic acidosis during exercise in humans and in ischemic murine models [34,35]; however, its role as a causal agent has been questioned in recent years [36,37]. Based on these critical assessments, we propose that the current interpretations can be summarized as follows:

- As the end-product of glycolysis, lactate is not merely a waste product formed under anaerobic [sic] conditions in muscle cells during physical exertion (i.e., physiological conditions). Instead, it is a metabolite continuously produced and removed at varying rates [7,28].
- Lactate concentration depends on the balance between its rate of production and removal, referred to as lactate turnover [38]. In this context, the concept of the "anaerobic threshold" has been challenged, as lactate is continuously produced under fully aerobic conditions and represents a marker of metabolic strain, rather than merely an indicator of oxygen depletion (e.g., during exercise) [7,38].
- Contrary to earlier beliefs, lactate serves as an energy substrate during exercise, providing fuel not only to muscle cells but also to other cell types, such as myocardial cells, neurons, and hepatocytes [10,33].

- The concept of the lactate shuttle represents a revolutionary framework for understanding lactate's role as a critical metabolic fuel [39]. This mechanism, enabled by Monocarboxylate Transporter (MCT) proteins, facilitates lactate transport across cell membranes into the bloodstream or into cells, depending on the specific MCT isoform (**Figure 2**). The lactate shuttle includes two key mechanisms: i) The intracellular lactate shuttle, where certain cells (e.g., type I muscle fibers) can oxidize lactate within their mitochondria; and ii) the cell-to-cell lactate shuttle, which transfers lactate between cells, such as from type IIX to type I muscle fibers [39,40].

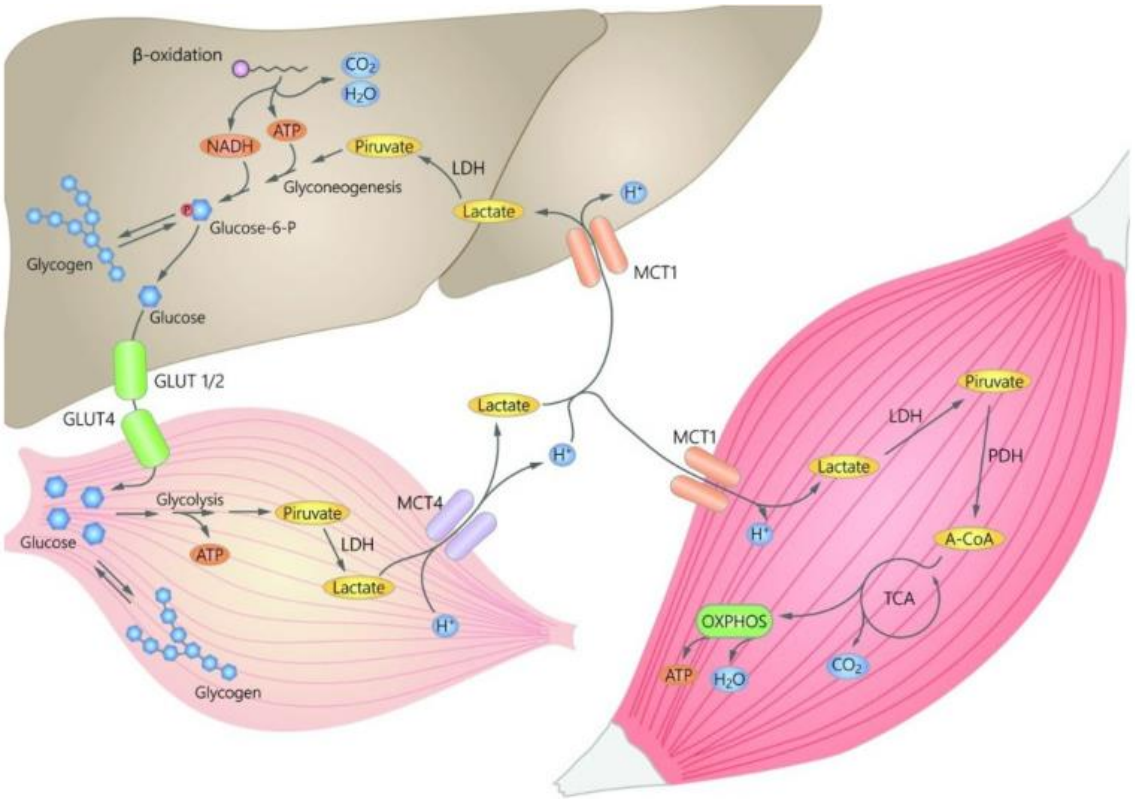

Figure 2. Schematic representation of the link among glycolysis, Cori's cycle, and lactate oxidation complex proposed in the lactate shuttle hypothesis.

This hypothesis explains the exchange between driver cells of lactate production and recipient cells of lactate consumption, which occurs within and among cells, tissues, and organs. For physical exercise, fast-twitch muscle fibers (driver) produce lactate from glycolysis and express MCT4 at the sarcolemma for lactate export, whereas slow-twitch oxidative and fast-oxidative glycolytic fibers (consumers) express MCT1 in the sarcolemma and mitochondrial reticulum for lactate import and oxidation. On the other hand, some lactate travels through the bloodstream and is taken up in the liver, where it is converted back to glucose. LDH: L-lactate dehydrogenase, MCT4: Monocarboxylate transporter 4, MCT1: Monocarboxylate transporter 1, PDH: Pyruvate dehydrogenase complex, TCA: Tricarboxylic acid cycle, A-CoA: Acetyl coenzyme A, OXPHOS: Oxidative phosphorylation, NADH: Reduced form of nicotinamide adenine dinucleotide (NADH+H+), ATP: Adenosine triphosphate. Reproduced from Ramírez de la

- Research from recent decades has challenged the notion of lactic acid formation and subsequent lactic acidosis under physiological pH. Glycolysis produces pyruvate (not pyruvic acid), which is then converted to lactate (not lactic acid) [36].
- Lactate plays an essential role in the acid-base balance. However, unresolved controversies persist, particularly regarding lactate's influence on metabolic acidosis during physical effort, with a lack of consensus among leading researchers in this field [36,37].
- Lactate acts as both a myokine and an exerkine, functioning as a signaling molecule with autocrine, paracrine, and endocrine effects [42]. It is involved in processes such as mitochondrial biogenesis, redox regulation, and adaptations to physical exercise, highlighting its role in energy metabolism and cellular signaling in various physiological. It is also plausible to suggest that exercise and the microbiota regulate systemic and brain levels of lactate [43]. For instance, *Veillonella atypica*, *Eubacterium hallii* group, *Anaerobutyricum hallii*, *Anaerostipes*, and other lactate-utilizing bacterial species produce short-chain fatty acids and other intermediates that enhance microbial diversity and enrich specific bacterial populations following an exercise period [44].
- Notably, lactate is a stress-associated signaling molecule and, in fact, could be considered as a "troubleshooter" metabolic hub, playing a critical role in allodynamic responses under both healthy and pathological conditions [45]. This underscores its relevance as a biomarker in exercise and sports physiology, due to its positive correlation with exercise intensity and stress levels, as previously reported by our research group [46].

5. Interaction and contribution of energy systems during maximal effort: Misinterpretations leading to conceptual errors

The study of interrelationships and contributions of energy systems began in the 1960s, spearheaded by Dr. Fox and collaborators [47]. Using ventilatory gas analysis and blood lactate measurements, they addressed the concept of the "energy continuum". However, this work led to some misunderstandings among exercise professionals and coaches. Specifically:

- That energy systems respond to the demands of intense exercise in a progressively sequential manner over time.
- That the "aerobic system" responds "slowly" to energy demands and plays a minimal role in short-duration performance. It was often suggested that the aerobic system only becomes predominant after approximately 2.5 min of exercise.
- From a cellular perspective, there is a delicate and complex interaction between energy systems, particularly in tissues with high metabolic demands, such as muscle fibers. This interaction highlights that metabolism cannot be segmented or dichotomized into isolated pathways, since the systems work in coordination to meet energy requirements.

The following points are proposed for an updated view: i) Energy systems do not activate sequentially because they are never entirely "off". Instead, the activity of various pathways is accelerated by specific metabolic regulatory factors (via allosteric regulation, accumulation of metabolic by-products, hormonal action, and chemical mediators of energy homeostasis); and ii) the global predominance of an energy pathway—the time during which a given metabolic pathway contributes proportionally more ATP than others during exercise—depends on several variables. These include training load (e.g., intensity), the recruitment of specific muscle fibers (which are metabolically specialized, such as glycolytic type IIX fibers and oxidative type I fibers), and the availability of energy reserves and substrates.

Regarding this updated view, exercise scientists and sports training professionals are encouraged to adopt the following terminology, previously proposed by Chamari and Padulo [6]:

- Explosive efforts (up to ≈ 6 s): Predominantly utilize the phosphagen pathway.
- High-intensity efforts (between >6 s to ~1 min): Predominantly utilize the glycolytic pathway.
- Endurance efforts (exercise bouts lasting >1 min): Predominantly utilize the oxidative phosphorylation pathway.

It is important to note that this classification applies to all-out efforts, i.e., maximal-intensity exercise sustained from start to finish (**Figure 3**).

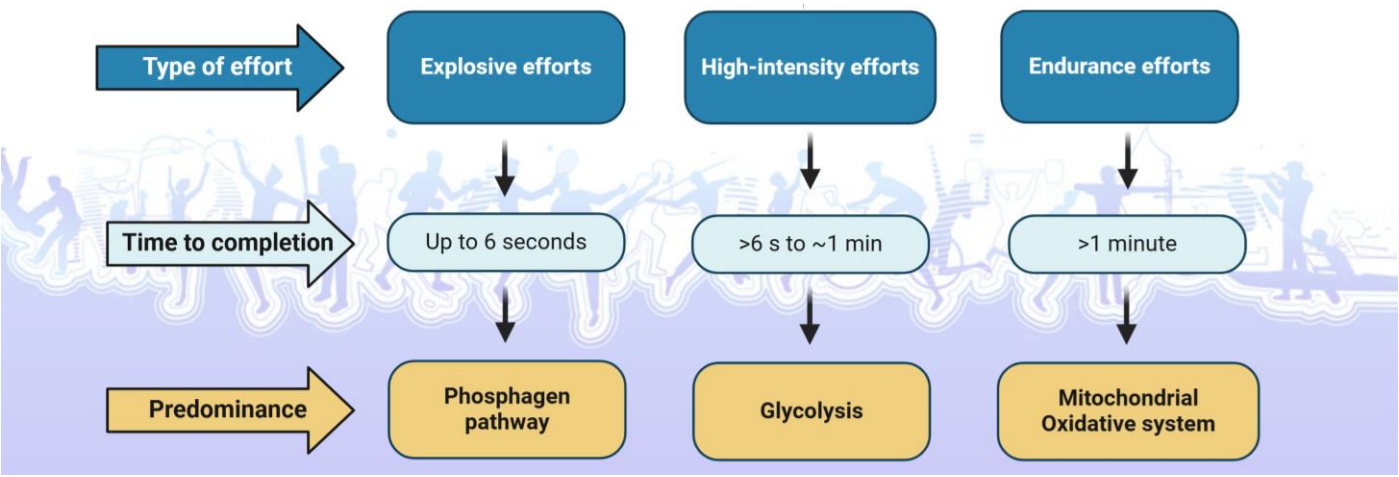

Figure 3. Predominance of energy metabolism based on the duration of all-out physical efforts [6]. This classification highlights the predominance of specific metabolic pathways depending on the duration and intensity of maximal efforts sustained from start to finish. For explosive efforts (~6 s), the phosphagen pathway predominates. High-intensity efforts lasting between 6 s and approximately one minute rely primarily on the glycolytic pathway. For endurance efforts exceeding one minute, the oxidative phosphorylation pathway becomes the dominant source of energy production.

Source: Created by the authors (D.A.B. and J.L.P.) with BioRender—https://biorender.com/ (accessed on 20 December 2024).

6. Conclusion

The terms anaerobic and aerobic for classifying physical efforts may be inadequate and imprecise, as they do not accurately represent the biochemical processes occurring under physiological conditions within muscle cells. The

predominance of energy systems, such as glycolysis, during certain physical efforts depends on energy demand and the regulatory mechanisms of metabolic pathways, rather than cellular anaerobiosis. Based on the evidence discussed in this article, it is proposed to classify energy systems into two categories: Extra-mitochondrial or oxygen-independent systems (i.e., phosphagen system and glycolysis) and the mitochondrial energy system. In the context of their duration and in "all-out" exercises, these efforts can be categorized as follows: i) Explosive efforts (lasting up to ~6 s), predominantly utilizing the phosphagen pathway; ii) high-intensity efforts (lasting > 6 s to ~1 min), primarily engaging the glycolytic pathway; iii) endurance or prolonged efforts (lasting over 1 min), where oxidative phosphorylation is the main contributor. Regarding lactate metabolism, a widely studied indicator in exercise biochemistry and physiology, its accumulation results from the balance between production and removal rates, rather than being a consequence of muscular "anaerobiosis" under physiological conditions. Currently, lactate is recognized as a valuable energy substrate that plays an important role in maintaining acid-base balance and potentially acts as a mediator in some of the adaptive responses of muscle cells to physical effort [39].

As lecturers and practitioners, we encourage the readers to consider these ideas, with appropriate application in context of the levels of organization of matter. Although exercise and health professionals working in the field insist that people understand terms such as "anaerobic" or "aerobic", the instructions may be more appropriately applied based on exercise intensity (e.g., to perform an explosive or high-intensity efforts). Complementary, when the aim is to explain at the molecular level, use intra- and extra-mitochondrial processes of energy production instead.

Finally, as editors of high-impact scientific journals, including the special issue "Exercise Biochemistry and Cellular Physiology: Mechanisms and Insights" in *Molecular & Cellular Biomechanics*, we invite the scientific and academic community (including students from sport sciences and nutrition programs) [48] to use the suggested terminology of this article as well as to submit their work in exercise biochemistry and cellular physiology, following the recommendations outlined in the PRESENT [49] and PERSiST [50] guidelines as extensions of CONSORT and PRISMA for clinical trials and systematic reviews with meta-analyses in sports sciences, respectively. In addition, we hope that students and professionals from the health sciences also incorporate these recent concepts into their current terminology [51]. These concepts are also key for several aspects related to human diseases [52].

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