GIULIA MAGRI RIBEIRO

O impacto das condições ambientais na diversidade taxonômica e funcional de amebas tecadas.

The impact of environmental conditions on taxonomic and functional diversity of testate amoebae

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Resumo

RIBEIRO, Giulia Magri. **O impacto das condições ambientais na diversidade taxonômica e funcional de amebas tecadas.** 2023. 352 f. Dissertação (Doutorado em Zoologia) – Instituto de Biociências, Universidade de São Paulo, São Paulo, 2023.

Os eucariontes microbianos, incluindo os chamados protistas, desempenham um papel crucial na manutenção dos ecossistemas globais. A qualidade dos ambientes é essencial na definição das comunidades de organismos que os ocupam e é influenciada por fatores como temperatura, salinidade, pH, níveis de oxigênio e a comunidade de organismos já presentes. Os organismos podem impactar positivamente o meio ambiente por meio de processos como decomposição, ciclagem de nutrientes e criação de habitat, enquanto a destruição e a poluição do habitat têm efeitos adversos. As atividades humanas aumentaram a frequência e a intensidade dos estressores ambientais, exacerbando seus efeitos. As amebas tecadas, particularmente do grupo Arcellinida, exibem vários graus de tolerância ao estresse e podem servir como bioindicadores. Este estudo visa compreender as respostas a nível de comunidade e individual desses organismos a dois estresses específicos: contaminação por arsênico e eutrofização/baixo teor de oxigênio. Este estudo combinou a caracterização funcional por meio de perfis de expressão gênica e compreensão mecanicista e evolutiva usando bioinformática. Demonstramos a expressão constitutiva dos metabolismos de resistência em *Arcella uspiensis* e sua capacidade de se ajustar a condições estressantes. Através de árvores filogenéticas, demonstramos também as múltiplas rotas de aquisição de genes de resistência ambiental. Além disso, desenvolvemos um pequeno estudo estratégias de metabarcoding para explorar adaptação e resistência ambiental no nível da comunidade. Ampliamos o banco de dados de marcadores COI e conduzimos um estudo de metabarcoding, obtendo informações sobre a diversidade, biogeografia e potencial de Arcellinida como bioindicadores. Isto porque, identificamos que as propriedades físico-químicas dos ambientes amostrados foram importantes determinantes da composição da comunidade de Arcellinida. Além disso, iniciamos o desenvolvimento de técnicas aplicadas, como PCR quantitativo em tempo real (qPCR) dos genes de resistência usando *Arcella uspiensis* como organismo modelo. A diversidade de estratégias entre as diferentes linhagens na adaptação às condições de arsênico e baixo teor de oxigênio, com variações nos mecanismos de resistência, é crucial para a compreensão das adaptações específicas e suas consequências, particularmente para microrganismos eucarióticos. Concluimos que *Arcella uspiensis* possui um arcabouço básico de resistência constitutivamente expresso refletindo em sua capacidade de se adaptar a condições estressantes e aumentar as chances de sobrevivência. Também reconhecemos a necessidade de desenvolver o genoma e utilizar *Arcella uspiensis* como organismo modelo para futuras pesquisas.

Palavras-chaves: Arcellinida, Bioindicadores, Contaminação por arsênio, Baixo oxigênio, Metabarcoding, Perfil de expressão gênica, Árvores filogenéticas, Metabolismos de resistência.

Abstract

RIBEIRO, Giulia Magri. **The impact of environmental conditions on taxonomic and functional diversity of testate amoebae.** 2023. 352 p. Dissertation (PhD of Zoology) – Biosciences Institute, University of Sao Paulo, Sao Paulo, 2023.

Microbial eukaryotes, including so-called protists, are crucial in maintaining global ecosystems. The quality of environments is essential in defining the communities of organisms that occupy them. Factors like temperature, salinity, pH, oxygen levels, and the community of organisms present influence the environment's quality. Organisms can positively impact the environment through decomposition, nutrient cycling, and habitat creation, while habitat destruction and pollution have adverse effects. Human activities have increased the frequency and intensity of environmental stressors, exacerbating their effects. Testate amoebae, particularly from the Arcellinida group, exhibit varying degrees of stress tolerance and may serve as bioindicators that reflect environmental conditions and the effectiveness of environmental actions. This study investigated the effects of multiple anthropogenic environmental stresses on testate amoebae. We aimed to understand these organisms' community and individual responses to two specific stresses: arsenic contamination and eutrophication/low oxygen. We combined community characterization using metabarcoding, functional characterization through gene expression profiling, and mechanistic and evolutionary understanding using bioinformatics. We demonstrated the constitutive expression of resistance metabolisms in *Arcella uspiensis* and its ability to adjust to stressful conditions. We also demonstrate the multiple acquisition routes of environmental resistance genes through phylogenetic trees. In addition, we discussed the application of metabarcoding strategies to explore ecological adaptation and resilience at the community level. We expanded the COI marker database and conducted a small metabarcoding study, obtaining information on the diversity, biogeography, and potential of Arcellinida as bioindicators. We discovered that the sampled environments' physicochemical properties are important determinants of the composition of the Arcellinida community. Also, we started the development of applied techniques such as quantitative real-time PCR (qPCR) of resistance genes using *Arcella uspiensis* as a model organism. The diversity of strategies among different lineages in adapting to arsenic and low oxygen conditions, with variations in resistance mechanisms, is crucial for understanding specific adaptations and their consequences, particularly for eukaryotic microorganisms. We concluded that *Arcella uspiensis* has a constitutively expressed basic resistance framework reflecting its ability to adapt to stressful conditions and increase the chances of survival. We also recognize the need to develop the genome and use *Arcella uspiensis* as a model organism for future research.

Keywords: Arcellinida, Bioindicators, Arsenic contamination, Low oxygen, Metabarcoding, Gene expression profiling, Phylogenetic trees, Resistance metabolisms

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Sumário

1 Introduction

Microbial eukaryotes play a crucial role in the maintenance of global ecosystems. Most of the eukaryotic diversity is microbial. Previously, all microbial diversity was included in a single group called protists, which are nowadays spread in many evolutionary lineages (Figure 2) (BURKI et al., 2020). This diverse group of organisms includes algae, amoebae, ciliates, and flagellates life forms. These organisms have different ecological preferences and significantly impact various environmental processes. For example, photosynthetic protists spread out at least in five great lineages (Stramenopiles in SAR, Haptista, Cryptista, Archaeplastida, and Discoba). Photosynthetic protists are responsible for a significant portion of global primary production (BENOISTON et al., 2017; FIELD et al., 1998). Many microbial eukaryotes, such as slime molds, are essential to nutrient cycling and decomposition. Slime molds are also a name given to several unrelated microbial eukaryotes, but most are in the Myxogastria, Amoebozoa group (BROWN; SPIEGEL; SILBERMAN, 2009; BALDAUF; DOOLITTLE, 1997; FIORE-DONNO et al., 2010). Because of their morphology and function in decomposition, they were previously classified as Fungi, but we know they are more related to amoebae. They are essential in breaking down dead organic material and recycling nutrients, contributing to environmental nutrient cycling. Other critical ecological functions that microbial eukaryotes act on are in parasitic and symbiotic interspecific relations. One example of parasitic protists is *Plasmodium*, the causative agent of malaria. *Plasmodium* is a member of Apicomplexa in the SAR group (Figure 2). Malaria is a widespread and significant global health problem, particularly in tropical and subtropical regions (ORGANIZATION et al., 2008; COWMAN et al., 2016). Finally, an actual example of symbiotic protists is zooxanthellae, which form a symbiotic relationship with corals, necessary for their survival through nutrients and energy providing. Disruption of the balance in the zooxanthellae algae and the coral relationship leads to a phenomenon known as coral bleaching and eventual death of the coral (MULLER-PARKER; D'ELIA; COOK, 2015; FOURNIER, 2013). In summary, microbial eukaryotes contribute significantly to maintaining global ecosystems through their involvement in primary production, food web dynamics, nutrient cycling, decomposition, and symbiotic and parasitic relationships. Their ecological functions are integral to the overall health, stability, and functioning of terrestrial and aquatic ecosystems.

1.1 Microbial diversity and model organisms

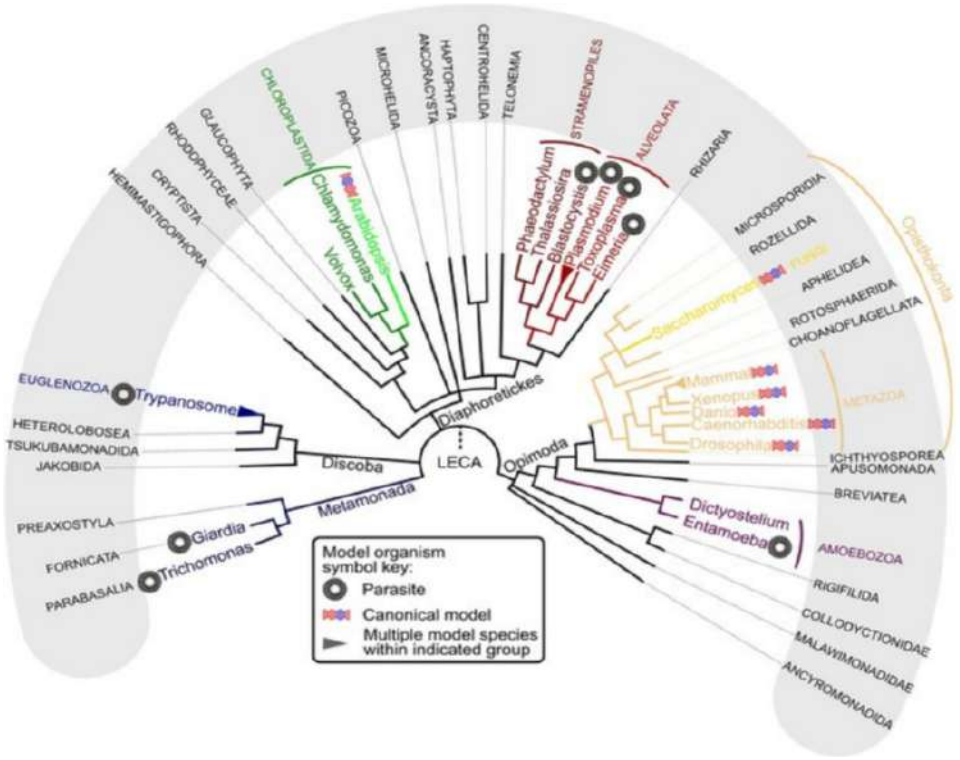
We always use living beings for our studies and experiments. For example, Mendel's laws use peas as a study model, and we have been model organisms for studies of human health and anatomy (IRION; NÜSSLEIN-VOLHARD, 2022). The term model organism was formalized late, in 1990, in the context of the genome project (DIETRICH; ANKENY; CHEN, 2014). For the funding agencies such as the National Institute of General Medical Sciences (NIH), an interesting "model"are "research organisms useful to understand fundamental aspects of biology, which are common to all organisms, including humans[a] (⟨https://www.nigms.nih.gov/education/fact-sheets/Pages/using-research-organisms.aspx⟩). The human genome project was a gigantic initiative that required a lot of licenses, financing, and standardization of protocols (COLLINS; MCKUSICK, 2001). In that way, a model organism was defined as a "Non-human species used to understand a biological phenomenon", which consists of using a simpler and more treatable organism to facilitate the experiments. Nowadays, the diversity of model organisms is much more restricted (Figure 1). At the begging of this tradition of using "models"to study, the diversity of organisms used was wider. For example, Lavoisier, in 1770, used guinea pigs to study metabolism and discovered the generation of heat through respiration (KAIYALA; RAMSAY, 2011). He built a system that placed the guinea pig wrapped in ice, and according to the melting rate of the ice, he was able to estimate how much heat was emitted by the animal and its metabolism rate.

1.2 Distribution of model organisms in the diversity of eukaryotes.

The classification of eukaryotes has undergone significant revisions, rendering the traditional five kingdoms taught in schools outdated. Presently, the diversity of eukaryotes is categorized into major lineages that extend beyond the commonly recognized animals, plants, and fungi, constituting only a fraction of this diversity (BURKI et al., 2020). Animals and fungi are now grouped within the Opisthokonta lineage, encompassing various single-celled lineages. Similarly, plants are classified within the Archaeplastida lineage alongside an extensive array of algae encompassing green, red, and cyano varieties. Notably, the remaining lineages depicted in Figure 1 primarily comprise ancient protists, representing a multitude of organisms that were previously not accorded distinct lineages.

These lineages have evolved independently, resulting in a diverse array of organisms with significant evolutionary distinctions.

Figura 1 – Model organisms distribution



Source: Hashimi H (2019) A parasite's take on the evolutionary cell biology of MICOS. PLoS Pathog, 15(12): e1008166. https://doi.org/10.1371/journal.ppat.1008166

An evident concern arises regarding the bias towards model organisms, which predominantly focus on plant and animal lineages, disregarding the vast diversity within protists (Figure 1). The utilization of protist models is mostly limited to cases involving parasites responsible for human diseases, where their study becomes imperative. Nevertheless, a notable exception exists within the Amoebozoa group, specifically in the case of *Dictyostelium discoideum*. Despite being a unicellular amoeba, it is a valuable model organism for investigating multicellularity in protists (ANNESLEY; FISHER, 2009). *Dictyostelium discoideum* undergoes a well-characterized life cycle that includes both unicellular and multicellular stages. When deprived of food, these organisms exhibit a remarkable behavior wherein they gather, aggregate, and transition into a multicellular form, actively searching for nourishment. They exhibit slug-like locomotion, resembling the movement of organisms in the environment as they seek food. They can also form fruiting bodies akin to fungi, dispersing a portion of their cells to more favorable locations with abundant food resources. Overall, the unique characteristics and experimental advantages of Dictyostelium

discoideum make it a powerful model organism for addressing fundamental biological questions, including cellular differentiation, aggregation, multicellular development, and morphogenesis.

Establishing a list of relevant organisms for scientific studies involves careful consideration and selection based on specific research objectives and requirements. However, this selection process often results in a disregard for the remaining biodiversity. This neglect of non-model organisms raises questions regarding the significance of investing efforts and resources in studying them. For instance, investigating non-model organisms can provide valuable insights into various biological phenomena, such as regeneration, which may not be effectively understood by studying human or animal tissues alone. While human and animal tissues exhibit regenerative capabilities, they may not possess the optimal mechanisms for efficient regeneration. Conversely, certain non-model organisms, like the ciliate *Stentor*, exhibit rapid and robust regenerative abilities, making them ideal models for studying regeneration (MARSHALL, 2021). Consequently, redirecting attention towards non-model organisms can offer unique opportunities for enhanced understanding and exploration of scientific questions.

1.3 Environmental Impact and Biodiversity

The quality of the environment is multifactorial and directly impacts the local biodiversity. Public health agencies define environment as the combination of physical, chemical, and biological factors that interact with the organism, affecting your development and survival (ORGANIZATION et al., 2020). Natural physical-chemical factors such as temperature, salinity, pH, and oxygen, interacting with biological factors such as the community of organisms already present in the environment, determine the characteristics of this specific environment and which type of organism it allows to shelter. Organisms can positively or negatively modify the environment. For example, organisms can positively impact the environment through decomposition, and nutrient cycling, such as Fungi and Myxogatria (CROWTHER; BODDY; JONES, 2012). Also, habitat creation, such as bromeliads, creates wetland environments for various species (LADINO et al., 2019). Other modifications of the environment have adverse effects on other organisms, such as habitat destruction and pollution. It is essential to recognize that the impact of organisms on the

environment can be complex and context-dependent. Understanding these interactions and their potential consequences is crucial for managing ecosystems, conserving biodiversity, and promoting the survival of multiple lineages.

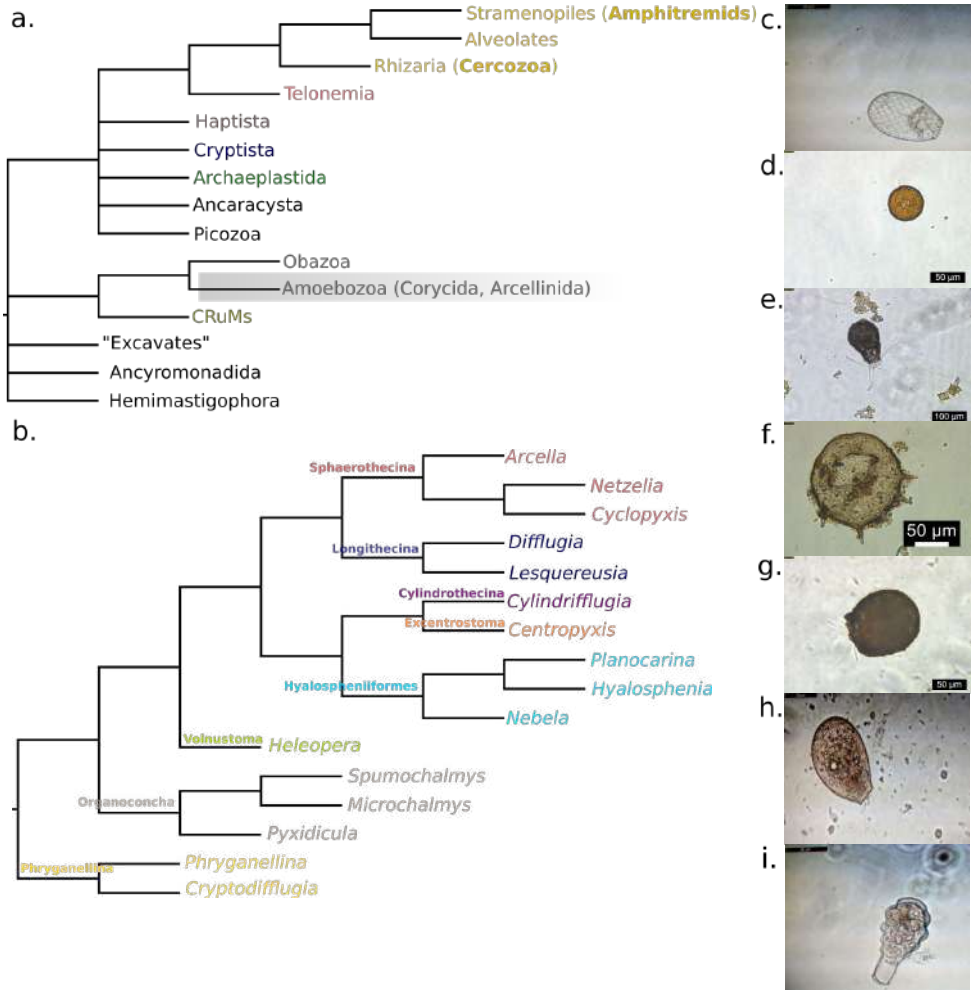
Stress caused by environmental conditions has always existed, but anthropic activity increased stressful events' frequency and exacerbated its effects (CRUTZEN; STOERMER, 2021; STEFFEN et al., 2007). In contemporary times, extending our discussions beyond natural stressors and addressing the broader concept of environmental impact has become imperative. Impacting the environment means any positive or negative alteration caused by anthropic activity. A few of the impactful actions of humanity are pollution, global warming, overconsumption of natural resources, and excessive human occupation of natural space. Although awareness of environmental impact is growing, combating humanity's negative actions still needs to be more effective. For example, the latest United Nations environmental report pointed out that we are not accomplishing the goals for sustainable development (SACHS et al., 2022). The established goal in the Paris Agreement was limiting global warming to a maximum of 2 degrees Celsius. We will not accomplish that goal in the current scenario because we expect to reach up to 3 degrees of average warming by 2100. These reports show us that the world is heading toward environmental calamity. Moreover, one of the biggest problems in the anthropic impact is that before humanity starts to feel these impacts, all the rest of the biodiversity will already be feeling them.

1.4 Testate amoebae as models for studies of environmental impact

Testate amoebae are a group of amoeboid protists that construct and inhabit a protective shell or test. Testate amoebae are a polyphyletic group of organisms with different evolutionary histories, present in at least three major lineages of eukaryotes (Rhizaria, Stramenopiles, and Amoebozoa) (Figure 2) (KOSAKYAN et al., 2016). This work focuses on testate amoebae belonging to Amoebozoa, the Arcellinida. The traditionally most important character for Arcellinida taxonomy was the morphology of the shell. Arcellinida species vary in the form of the shell, as round, hemispherical, with spines or vase-shaped. Arcellinida shells also vary in size in a range of around 20 to 700 micrometers, accounting for gigantic species such as *Difflugia gigantea* (MEISTERFELD, 2002; MAZEI; WARREN, 2017; CHARDEZ, 1967). After the advance of molecular biology, morphology is no longer

enough to identify all species. After sequencing, we observed several examples of phenotypic plasticity, cryptic diversity, and convergence in Arcellinida (PORFÍRIO-SOUSA; RIBEIRO; LAHR, 2017; GONZÁLEZ-MIGUÉNS et al., 2022b; MULOT et al., 2017). Currently, the Arcellinida identification process needs to combine morphology and molecular biology. Using a phylogenomic approach, Lahr and collaborators subdivided Arcellinida into eight lineages (Sphaerothecina, Longithecina, Excentrostoma, Hyalospheniformes, Volnustoma, Organoconcha, and Phryganellina) (Figure 2) (LAHR et al., 2019). The knowledge and availability of data for the Arcellinida group are still very limited. We need to increase our databases and better integrate general biology, molecular biology, and ecology knowledge for this group.

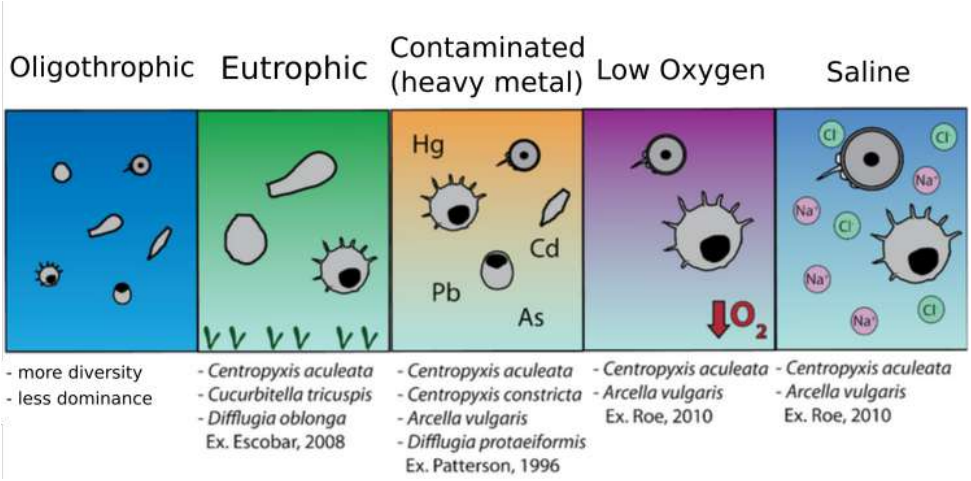
Figura 2 – Phylogenetic representations are positioning Arcellinida in the eukaryotic diversity. (a) Eukaryotic phylogeny based in the new tree of eukaryotes(BURKI et al., 2020). Different colors indicate major lineages of eukaryotes. Groups of testate amoebae found in the different lineages are named between parentheses. Arcellinida belongs to the Amoebozoa group indicated by the gray box. (b) Arcellinida phylogeny based in a phylogenomic reconstruction (LAHR et al., 2019) and SSUrDNA reconstruction (GONZÁLEZ-MIGUÉNS et al., 2022b). The different colors indicate Arcellinida lineages, defined by Lahr et al. and Gonzalez-Miguéns. (c-i) Examples of testate amoebae species. (c) *Euglypha sp.*, testate amoeba of the Rhizaria group. (d) *Arcella sp.* a Sphaerothecina. (e) *Zivkovicia sp.* a Longithecina. (f) *Centropyxis sp.* an Excentrostoma. (g) *Netzelia sp.* a Sphaerothecina. (h) *Nebela sp.* a Hyalospheniformes. (i) *Hyalosphenia elegans* a Hyalospheniformes



In a world where environmental impacts are increasingly evident, arcellinids are increasingly important in ecological and evolutionary studies. Arcellinida species are benthic protists with variable stress tolerance degrees being useful bioindicators. We commonly find arcellinids in freshwater lakes, mosses, and sphagnum terrestrial environments (MEISTERFELD, 2002; SMITH; BOBROV; LARA, 2009). Arcellinida species usually have narrow ecological preferences (MARCISZ et al., 2020). Despite this, some species are very

tolerant to stress conditions (ROE; PATTERSON; SWINDLES, 2010). We find Arcellinida species in highly impacted environments, such as road salt contamination, heavy metal pollution, and eutrophic (ROE; PATTERSON; SWINDLES, 2010; ROE; PATTERSON, 2014; PATTERSON et al., 2019; DANIEL; LOPES, 2006; REGALADO et al., 2018; JU et al., 2014; KOSAKYAN; LARA, 2019; SILVA et al., 2013; ORTIZ et al., 2009; CZAPLUK; RUTKOWSKI; RYBAK, 2018). Thus, we predict that in an environment with optimal conditions for the group, we should find a high richness of Arcellinids, with high evenness in the abundances (Figure 3). However, only a few lineages survive in more stressful environments, such as eutrophic environments, contaminated by heavy metals, hypoxic, and with variable salinities. The most resistant lineages of arcellinids are from the genus *Arcella*, and *Centropyxis* (ROE; PATTERSON; SWINDLES, 2010; ROE; PATTERSON, 2014; PATTERSON et al., 2019; DANIEL; LOPES, 2006; REGALADO et al., 2018; JU et al., 2014; KOSAKYAN; LARA, 2019; SILVA et al., 2013; ORTIZ et al., 2009; CZAPLUK; RUTKOWSKI; RYBAK, 2018). In that way, in stressful environments, we should find low evenness, with some species being dominant in the testate amoebae community. What makes some species of Arcellinid more resistant than others is still a mystery. However, Arcellinids are currently used as bioindicators and in monitoring freshwater environments (ARRIEIRA et al., 2015; ATASIEI et al., 2022; NASSER et al., 2020; ROE; PATTERSON; SWINDLES, 2010). Their main advantages as a study model are that they are easy to find and have low-cost work. An essential characteristic of bioindicator species is that they have apparent differences in resistance and respond quickly to environmental changes. Thus, using Arcellinids in bioindication can inform public and management policies, for example, the quality of the environment and the effectiveness of environmental actions, allowing to plan and re-plan actions quickly and efficiently.

Figura 3 – Examples of variations in the Arcellinid community due to environmental conditions. The size of the shell represents dominance in the community. Under oligotrophic conditions, we should find higher richness and less abundance. However, in other conditions, the surviving species dominate the community.



1.5 Molecular biology and testate amoebae ecology

Molecular biology allowed us to advance a lot in the knowledge of biodiversity and its characteristics. Currently, high-throughput sequencing technologies are the revolution that allows the exploration of neglected groups of organisms at the community and individual levels. Arcellinids are single-cell organisms, many species do not grow in cultures, and many species are not that abundant in the environment. In that way, many kinds of studies, for example, genetic and functional studies, are more complicated to develop with this group. One negative implication was that we lacked a lot of knowledge of basic biology and the evolution of this group. Omics technologies opened new possibilities for discovery for Arcellinida. For the community level, metabarcoding permits the sequencing of markers directly from environmental DNA samples, revealing hidden diversity and characterizing the local communities (LINDEQUE et al., 2013; GONZáLEZ-MIGUéNS et al., 2023). For individual-level studies, transcriptomics, and in some cases genomics, permits exploration through comparative analysis of species characteristics, such as trait evolution, ecology, and physiology (LIU et al., 2017; ZOU; ZHANG; GONG, 2020; FENG et al., 2022; RIBEIRO; LAHR, 2022). Single-cell omics were a revolution for microbial eukaryotes studies because they allow us to discover new unculturable diversity and distinguish species in groups with little data produced (SIERACKI et al., 2019; BLAXTER et al., 2022; SEYFFERTH et al., 2021; LIU et al., 2017). For example, there is still no Arcellinid genome available. Thus, we

have already answered evolutionary and ecological questions by exploring transcriptomes independent of a reference genome. For example, without a genome, we already started to untangle the systematics of the group, describing resistance metabolisms, reproduction, and life cycle (RIBEIRO; LAHR, 2022; LAHR et al., 2019; HOFSTATTER; LAHR, 2019; RIBEIRO et al., 2020). In summary, we should keep investing in sequencing genomes and transcriptomes of microbial eukaryotes, as there is still a lot of undiscovered diversity in these groups and many ecological, physiological, and evolutionary unanswered questions.

1.6 Progress in the study of Arcellinida using Arcella uspiensis as model.

Arcella uspiensis is an Arcellinida species for which we can establish stable cultures and from whom we already developed a lot of basic biology and protocols knowledge until now. In our first paper using this model organisms in 2017, we discovered that two different morphotypes of *Arcella* were the same genetic unity (PORFÍRIO-SOUSA; RIBEIRO; LAHR, 2017). We also observed that the shape of the shell changed when they were put in cultures. Unifying those two discoveries, we claimed that *Arcella* has phenotypic plasticity according to the environment they are living. In our next paper of 2018, we described the culture and growth cultures protocol developed with *Arcella uspiensis* (RIBEIRO et al., 2019). This protocol has a lot of relevance because it is replicable, and we could use it for ecological experiments. In this thesis, in Chapters 3 and 5, we performed low oxygen and arsenic transcriptomic experiments. Using RNA-seq, we could leap forward in our knowledge of Arcellinida and *Arcella uspiensis*. In our 2019 paper, we clarify the systematics and taxonomy of Arcellinids using a phylogenomic approach (LAHR et al., 2019). We have already applied this classification to trace gene and pathways evolution in Arcellinids, as in Chapters 2, 3, and 5. In our paper of 2020, we built the first reference transcriptome for Arcellinids, using 36 *Arcella uspiensis* transcriptomes produced in the laboratory (RIBEIRO et al., 2020). We annotated and described the main metabolic pathways of the group. We often use this reference to map our new *Arcella uspiensis* transcriptomes as the ones produced in Chapters 4 and 6. We also use them to fish marker genes for phylogenetic purposes, such as the SSU and COI genes, in Chapter 2. Other works from the laboratory described the shell formation process and meiosis using Arcellinida and *Arcella uspiensis* as models (HOFSTATTER et al., 2016). In this way, before my

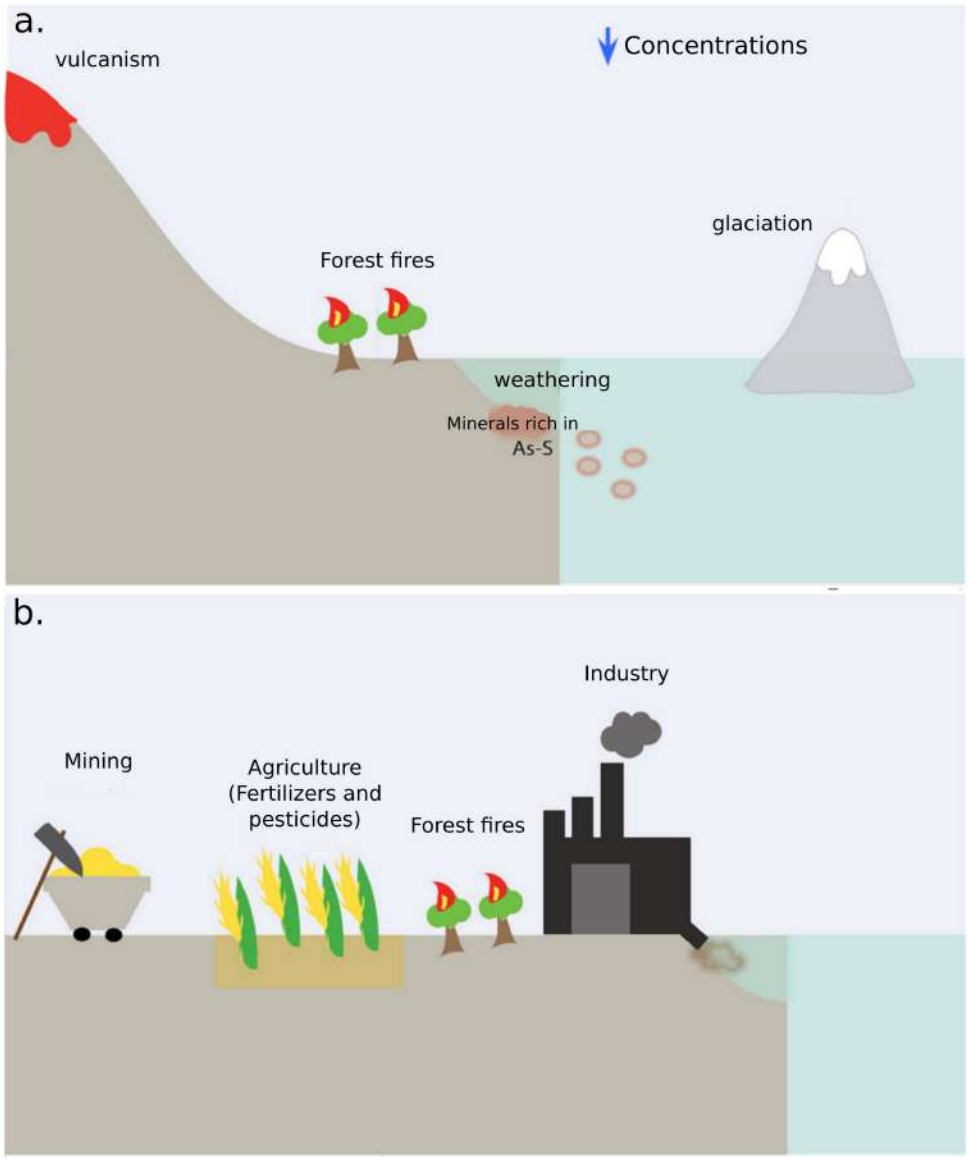
Ph.D., we already made significant advances in understanding the basic biology of *Arcella uspiensis* and developed a lot of protocols with the group.

In this dissertation, we were interested in resistance metabolisms in Arcellinida. From the ecological investigation, we knew that Arcellinida has a variable resistance capacity between species (ROE; PATTERSON; SWINDLES, 2010; NASSER et al., 2014). Also, from my previous works from the master's degree (RIBEIRO et al., 2020), we knew that a few Arcellinida species might have pathway characteristics of more resistant lineages. In that way, we explored two issues related to environmental impacts and their effect on Arcellinids. We used transcriptomics techniques to study the gene expression of our "model"organism, *Arcella uspiensis*, subjected to conditions of arsenic contamination and low oxygen.

1.6.1 Arsenic lakes: why we should care

Arsenic in water bodies can be from a natural or anthropogenic source. Arsenic is a ubiquitous metalloid in the environment that always had an essential role in life history. The environment contains low concentrations of inorganic and organic arsenic-containing compounds from volcanism, forest fires, weathering of arsenic-rich minerals, and melting ice caps (Figure 4) (MORIN; CALAS, 2006). However, anthropic actions, such as mining activities and pesticide use, have the potential to modify the predominant form in the environment (Figure 4) (MORIN; CALAS, 2006). It is also characterized as endless contamination because even with water flow and sediment accumulation, the contaminant keeps returning to the water column (NIKOLAIDIS et al., 2004; PALMER et al., 2019). The reason for that is that arsenic has a sensitive reducing nature. Changes in the redox conditions caused by eutrophication and climate changes can mobilize arsenic to the water column (SENN; HEMOND, 2004; HASEGAWA et al., 2009; GALLOWAY et al., 2018). In Brazil, the legally admitted threshold for arsenic in water is 10 μg/L (CARVALHO et al., 2017). However, sites contaminated by mining activity can contain values that reach 90 times this threshold. Still, only the total arsenic concentration is usually measured, while the different types of speciation vary in toxicity.

Figura 4 – Examples of sources of (a) natural and (b) anthropic sources of arsenic contamination in the environment. In natural environments, arsenic is present in low concentrations. Anthropic action can increase arsenic concentration and change its forms and oxidative state through pollution.



The history of arsenic compounds accompanied the history of Earth, and organisms' metabolic adaptations could tell this history (Figure 5) (CHEN et al., 2020). The level of toxicity of arsenic is variable, according to its form and oxidation state (Figure 6). Inorganic arsenic is always more toxic than organic. Also, oxidized arsenic is always less toxic than the reduced forms (BARRA et al., 2000). However, the prevalent form of this arsenic changed throughout Earth's history. More toxic reduced arsenic was prevalent before the atmosphere's great oxidation event (GOE). However, the GOE makes less toxic oxidized forms more prevalent (Figure 6). The change in forms and oxidative state of arsenic left a clear signal in the biodiversity (CHEN et al., 2020). After the GOE, organisms had to

adapt their arsenic resistance pathways to deal with the oxidized form of arsenic. Although oxidized forms are less toxic, the organisms did not have the enzymes to metabolize them. In that way, arsenic resistance metabolisms amplified after the GOE (CHEN et al., 2020). The oxidized forms should still be more prevalent (Figure 6). Determining the type of arsenic speciation is a difficult and expensive procedure. Inorganic forms (3+ and 5+) are 100 times more toxic than organic forms, and inorganic arsenic 3+ is 60 times more toxic than inorganic arsenic 5+ (BARRA et al., 2000). Speciatiate arsenic relies on chromatography and electrophoresis for shape separation and spectrometry for quantification (RUKH et al., 2015). Thus, the characterization of bioindicator species would be most practical to show evidence of the presence of arsenic when diagnosing water quality. Within Arcellinida, there seem to be species in a gradient between the highly resistant to the least resistant (PATTERSON et al., 2019). Next-generation sequencing techniques favor the environmental ecology of testate amoebae because their morphological identification remains controversial, and the procedures are laborious, involving "manual"cell counting.

Figura 5 – Oxygen levels and arsenic speciation. The graph shows the relationship between oxygen levels on Earth and the prevalence of each form of arsenic. The horizontal and vertical axes represent geological time (in Gy) and oxygen levels (% atmosphere), respectively. The blue curve represents the Earth's oxygen level over time. The stars represent the emergence of some of the eukaryotic lineages. Note that several strains arose under conditions with lower oxygen levels. The exact curve of arsenic speciation over time has yet to be discovered. However, at lower oxygen levels, there is still a tendency to form reduced arsenic species.

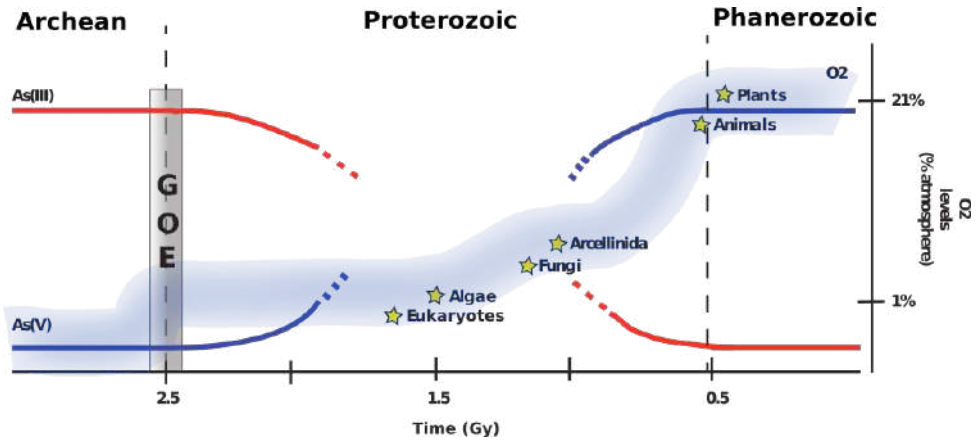
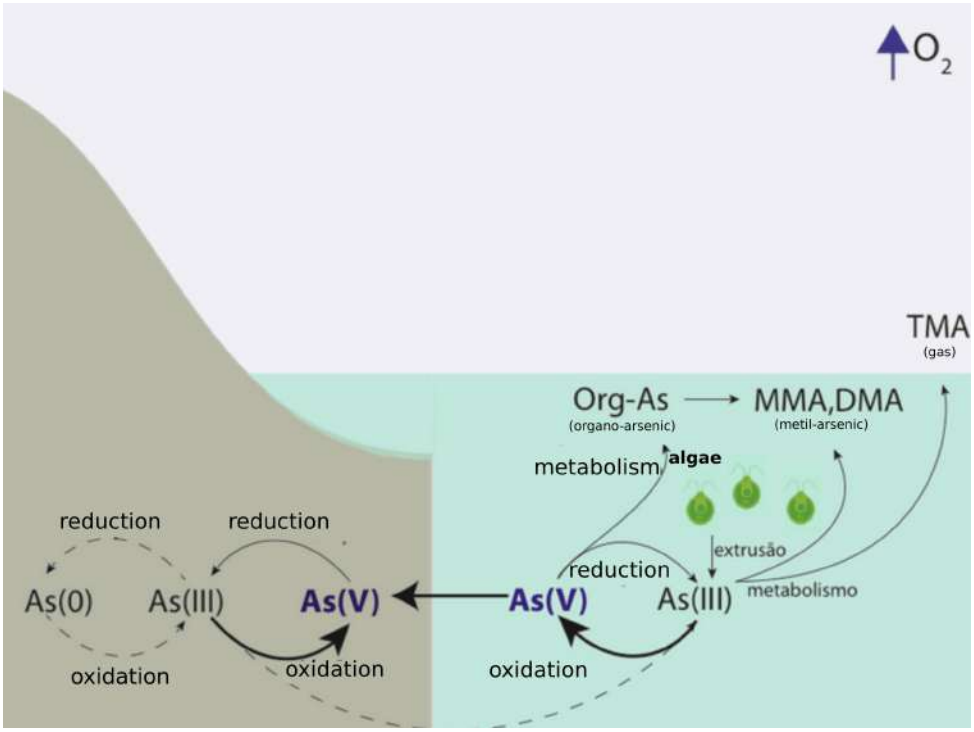


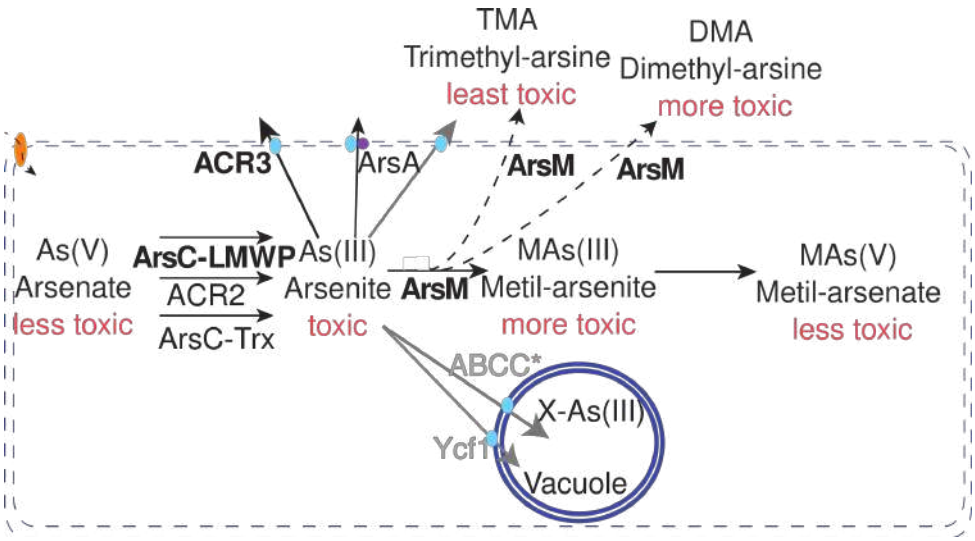
Figura 6 – Examples of forms and conversions of arsenic in the environment. Arsenic can be organic or inorganic-forming compounds. Also, it is possible to find it in your reduced or oxidized state. The environment directly affects that, for example, through oxygen levels in the atmosphere, where an oxidative atmosphere would make oxidate forms of arsenic more prevalent. Additionally, the metabolism of the organisms in the environment substantially alters the prevalent forms of arsenic compounds in the environment.



Arsenic has several toxicity factors for living organisms, such as reactive oxygen species formation, protein folding, and many other changes in gene expression, mutagenesis, and carcinogenesis (DING et al., 2009; JACOBSON et al., 2012; FLORA, 2011; HALTER et al., 2015). Because the atmosphere used to be reductive, arsenic resistance pathways developed first to metabolize and extrude the reduced forms and later to transform the oxidized forms into the reduced ones (Figure 7). Arsenic resistance pathways are ancient and did not change much along evolution (CHEN et al., 2020). However, the studied lineages are still very limited. Up to now, the studies of arsenic resistance pathways are for the bacterial domain and eukaryotes of economic interest (BHATTACHARJEE; ROSEN, 2007; SILVER; PHUNG, 2005; FEKIH et al., 2018). In bacteria and eukaryotes, arsenic cannot freely access the cell, passing through common membrane transporters (phosphate transporters) (ROSEN, 1990). Unprocessed arsenic compounds accumulate in the cell and generate the toxicity effects mentioned previously. The most ancient strategies for reduced inorganic arsenic are methylation to less toxic forms followed by extrusion (CHEN et al.,

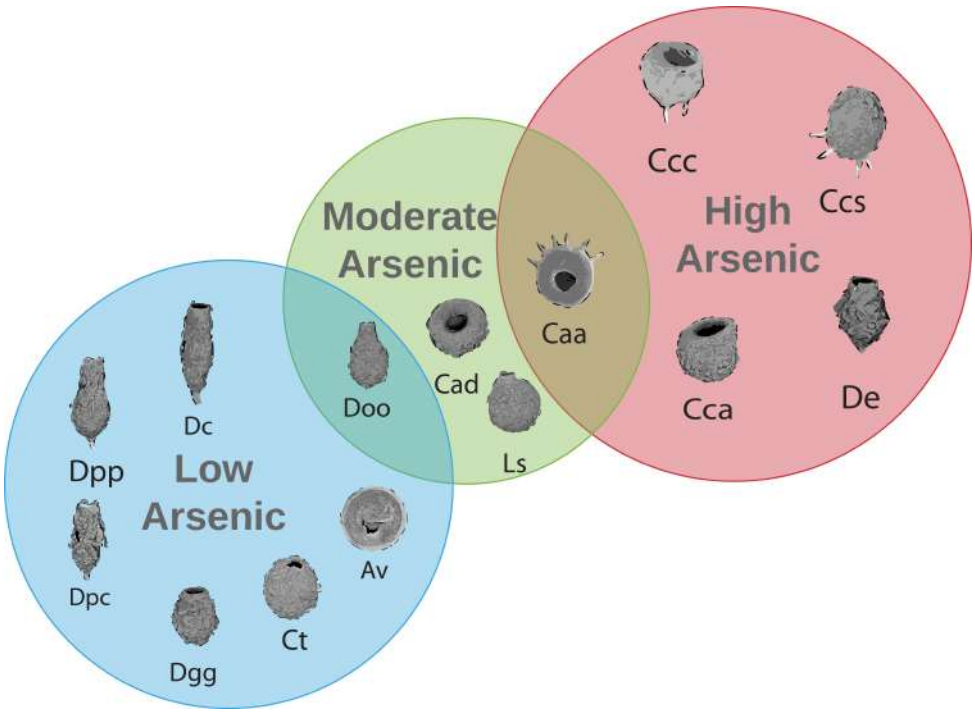
2020). Arsenite methyltransferases (ArsM) methylate inorganic arsenite, generating less harmful forms of arsenic, many of which do not accumulate through elimination in the form of gas (THOMAS et al., 2007; QIN et al., 2006). Arsenite transporters (Acr3 and ArsB) make the extrusion of arsenite, which expends energy for this function (ROSEN, 1990; GHOSH; SHEN; ROSEN, 1999). Before the GOE, methylation and extrusion of reduced forms were the most common resistance metabolisms. After GOE, as the oxidized form of arsenic became prevalent, arsenite reductases diversified and expanded (CHEN et al., 2020). Arsenate reductases are the class of enzymes that transforms oxidized inorganic arsenic (arsenate) into its reduced form (arsenite) (WU; SONG; BEITZ, 2010; MESSENS; SILVER, 2006). After transformation into the reduced form (arsenite), arsenite transporters extrude it. An additional pathway option, widely used in plants, is to sequester arsenite in vacuoles, reducing its effect on the cell environment (ZHANG; MARTINOIA; LEE, 2018; ZHAO et al., 2009). The strategy adopted is variable between lineages. Furthermore, the homology between many of these genes was still very uncertain for eukaryotes. Thus, understanding the ecological context, the homology of genes, and the evolution of these lineages would inform a better understanding of the metabolic evolution of these resistance pathways.

Figura 7 – Main enzymes in arsenic metabolism. Arsenic compounds are indicated, and their toxicity is colored red. Enzymes' names are beside the arrows. Enzymes that evolved before GOE are in bold. Arsenic accesses the cell through membrane channels, for example, phosphate channels in orange. Inorganic oxidized arsenic (arsenate) can be reduced to arsenite through arsenate reductase enzymes (ArsC, ACR2). Inorganic arsenite can be extruded through membrane transporters (ACR3, ArsB, MRPs). Alternatively, arsenite can be stored in vacuoles through transporters (Ycf1, ABCC). Finally, arsenite can be methylated through methyltransferases (ArsM) to organic, less toxic forms and forms that do not accumulate in the cell. ArsH can make the oxidation of organic methyl arsenite to less toxic forms.



For Arcellinids, we expect arsenic contamination to affect the amoebae and their prey (bacteria). Thus, one hypothesis about the pressure generated by arsenic in the amoebae community is that on top of the toxicity of arsenic to the amoebae, the shrinkage of bacterial diversity may also cooperate in excluding amoebae species more susceptible to stress due to nutritional deficiency (PATTERSON et al., 2019). At the community level, the works of Nasser and Patterson already inform us about the different degrees of resistance among Arcellinids (NASSER et al., 2016; PATTERSON et al., 2019) (Figure 8). Most *Difflugia* species are characterized by low resistance. Moreover, other species, such as *Centropyxis*, would be the most resistant to this arsenic. However, these ecological studies are still focused on morphology and need molecular confirmation, for example, genetic barcoding, which can more precisely characterize these communities. Also, the physiological mechanisms involved in arcellinids' resistance to arsenic are still a mystery.

Figura 8 – Main species of testate amoebae found in previous studies for each level in an arsenic contamination gradient. Dc - *Difflugia curvicaulis*; Dpp - *Difflugia proteiriformis proteiriformis*; Dpc - *Difflugia proteiriformis claviformis*; Dgg - *Difflugia glans glans*; Ct - *Cucurbitella tricuspis*; Av - *Arcella vulgaris*; Doo - *Difflugia oblonga oblonga*; Cad - *Centropyxis acuelata discoides*; Ls - *Lesquereusia spiralis*; Caa - *Centropyxis acuelata acuelata*; Cca - *Centropyxis constricta acuelata*; De - *Cylindrifflugia elegans*; Ccs - *Centropyxis constricta spinosa*; Ccc - *Centropyxis constricta constricta*. The images of the testate amoebae were taken from the works in which they were described in the arsenic gradients, to visualize what they classified in this species (NASSER et al., 2016; PATTERSON et al., 2019)

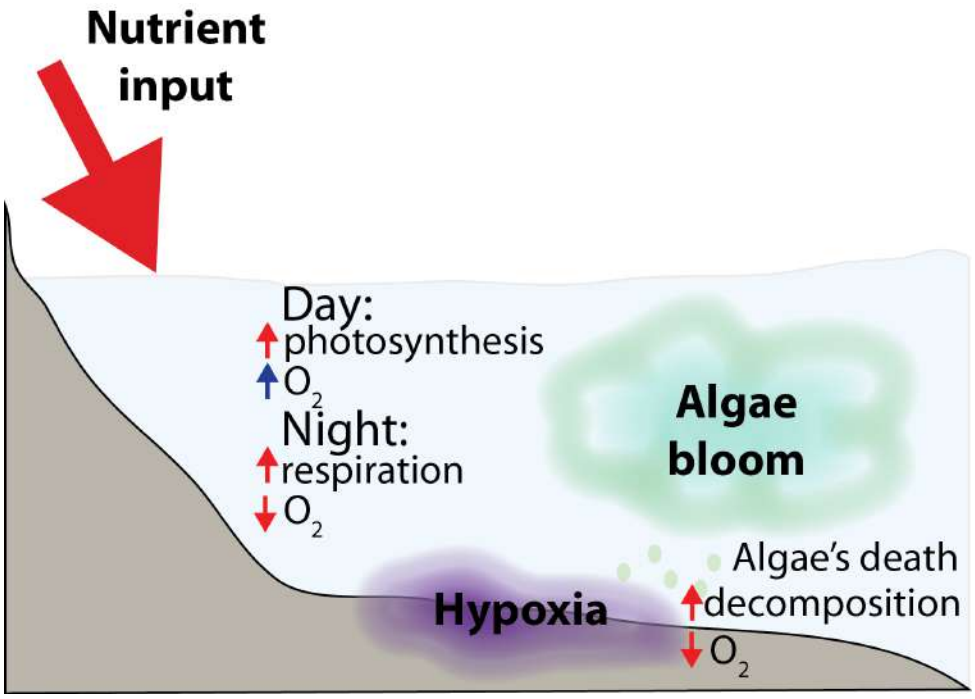


1.7 Eutrophication and low-oxygen

Eutrophication is a frequent condition developed in aquatic environments, characterized by exacerbated algae and bacterial reproduction due to nutrient excess (KHAN; ANSARI, 2005). The leading causes of eutrophication are anthropic, such as pollution, inappropriate waste disposal, and fertilizers. One of the significant consequences of eutrophication is a wide variation in the availability of oxygen in the medium. During the day, algae photosynthesis releases oxygen into the environment, increasing availability. However, during the night, the high rates of decomposition, mainly related to the death of algae added to the respiration of all organisms, can significantly reduce the oxygen available in the environment and generate hypoxic regions (TYLER; BRADY; TARGETT,

2009). These large fluctuations in oxygen are a stressor for communities, eliminating some of the less resilient species (ALEXANDER; VONLANTHEN; SEEHAUSEN, 2017; KHAN; ANSARI, 2005; HALE; CICCHETTI; DEACUTIS, 2016). In this work, we investigated the effect of eutrophication using lakes of urban and natural parks in Madrid. Urban lakes, although they represent a natural environment in the middle of large cities, are usually already environments with a tremendous anthropic effect. As they are located in the middle of big cities, they suffer from garbage disposal, contamination, the inclusion of animals by man, and eutrophication. Thus, investigating the effects of human occupation on urban parks landscapes represents an excellent opportunity to compare altered and pristine environments.

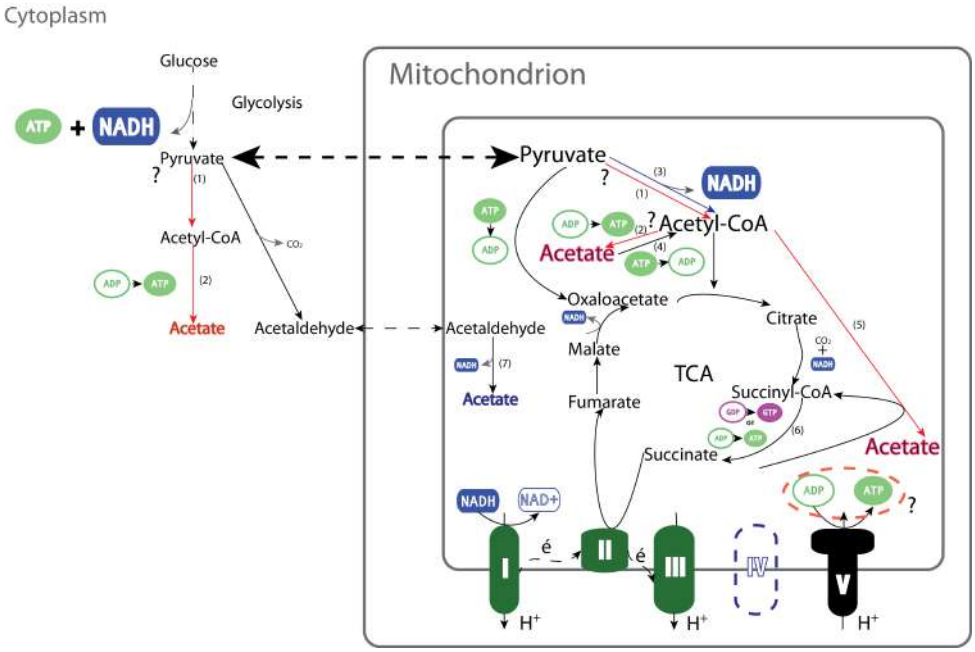
Figura 9 – Representation of a eutrophic lake environment. During the day, photosynthetic activity generates high levels of oxygen that accumulate. After a nutrient input, algae take advantage of this excess and over-reproduce in an algal bloom (green region). However, during the night, with respiration and decomposition, some regions can become hypoxic (purple regions). Usually, hypoxic regions form in the interface between sediment and water, a region with a greater density of organisms.



Many organisms can survive temporarily or live permanently in low oxygen conditions. Algae, for example, can maintain themselves during nocturnal periods of low oxygen (CATALANOTTI et al., 2013). Like algae, many other organisms can survive hypoxic conditions. Related mechanisms consist of metabolic regulations, mostly on energetic

metabolism (HWANG et al., 2020; ANTÓNIO et al., 2016; VIA et al., 1994). The fueling of the energetic metabolism depends mainly on glycolysis, a common pathway to all living organisms that converts glucose into pyruvate (RIGOULET et al., 2020; YELLEN, 2018). In this conversion process, the organism invests 2 ATP (energy-rich adenosine triphosphate) and generates 4 ATP, generating a final balance of 2 extra ATP. Compared to aerobic metabolism, it is a light output, where after going through the Krebs cycle and the phosphorylative chain, on average, aerobic respiring organisms generate 30-32 ATP. Current evidence points out that the glycolytic pathway might not sustain an organism on its own (YELLEN, 2018). More nutrients, cofactors, and organic composts would be needed to continue glycolysis. Thus, organisms in low oxygen conditions have developed solutions to recover cofactors and substrates or generate additional energy yield. For example, the fermentation pathways that make the recovery of cofactors more efficient, such as alcohol, aldehyde, and lactate fermentation pathways (RIGOULET et al., 2020). Also, additional shuttles, malate–aspartate shuttle (MAS), recover pyruvate, the primary substrate for the fermentations (YELLEN, 2018). The use of parts of the TCA cycle, maintaining partial functioning of OXPHOS (ZHENG, 2012). All of that would make viable survival based on glycolysis. Another pathway, most common in obligatory or facultative anaerobes, uses the conversion of acetyl-CoA to acetate to generate energy (STAIRS; LEGER; ROGER, 2015; MÜLLER et al., 2012). Some lineages of algae, such as *Chlamydomonas* for example, have this metabolic flexibility, using the aerobic and photosynthetic pathways during the day. They activate the anaerobic metabolism at night, with glycolysis and ASCT acting (CATALANOTTI et al., 2013). There are several other regulations and adaptations to low oxygen, and the solutions found by the organisms are also variable. However, we believe the diversity of strategies among lineages must be closely related to their degree of resistance. How this variation occurs, and its consequences is still a new and developing area, especially for eukaryotic microorganisms.

Figura 10 – Scheme representing essential reactions of low oxygen energy metabolism common in eukaryotes. The enzymes represented here are not necessarily present in all organisms. Enzyme names: (1) pyruvate:ferredoxin oxidoreductase (PFO); (2) FeFe-hydrogenase; (3) acetyl-CoA synthetase (ACS); (4) pyruvate dehydrogenase (PDH); (5) Acetate-CoA ligase (ACS); (6) acetate:succinate CoA transferase (ASCT); (7) succinyl-CoA synthetase (SCS); (8) Aldehyde dehydrogenase (ALDH); (9) Alcohol dehydrogenase (ADH). We also represented the other components of the TCA cycle and electron transport chain from aerobic mitochondria. Exclusively anaerobic enzymes are colored in red, and anaerobic processes of cofactors recovery are colored in gray.



1.8 Question, hypothesis, objectives

Considering the above, we analyze the effect of multiple anthropogenic environmental stresses on testate amoebae in this work. We studied the evolutionary history of stress responses in Arcellinids and individual responses through gene expression. We evaluated two different pressures, arsenic contamination and eutrophication/low oxygen. Our overall research objective is to understand who lives in these conditions and how they live. To work on this issue, we: (i) characterized the specific pathways related to the resistance pathway using bioinformatics; then (ii) we untangled the mechanistic through gene expression profiles using *Arcella uspiensis* as a model organism, grown under the investigated stress.

Dissertation statement: Ecological studies have shown that Arcellinida are present in environments with low oxygen levels and contaminated by arsenic. Their survival under these pressures must be related to metabolic adaptations. Arsenic resistance is mostly related to specific pathways of detoxification and extrusion. Fermentative pathways are fundamental for survival in low-oxygen environments, and these resistance pathways are related to maintaining the environmental community.

1.9 Hypothesis

(i) The molecular evolution of arsenic metabolic genes will elucidate the history of the adaption of testate amoeba to arsenic.

(ii) Highly tolerant testate amoeba lineages have specific biochemical pathways and gene expression profiles related to resistance.

(iii) Species that build stable populations in eutrophic lakes use fermentative metabolism to tolerate oxygen fluctuations.

(iv) Tolerant species up-regulate fermentative pathways in microcosms under low oxygen pressure.

1.10 Objectives

(i) Characterize molecular evolution of known arsenic resistance genes;

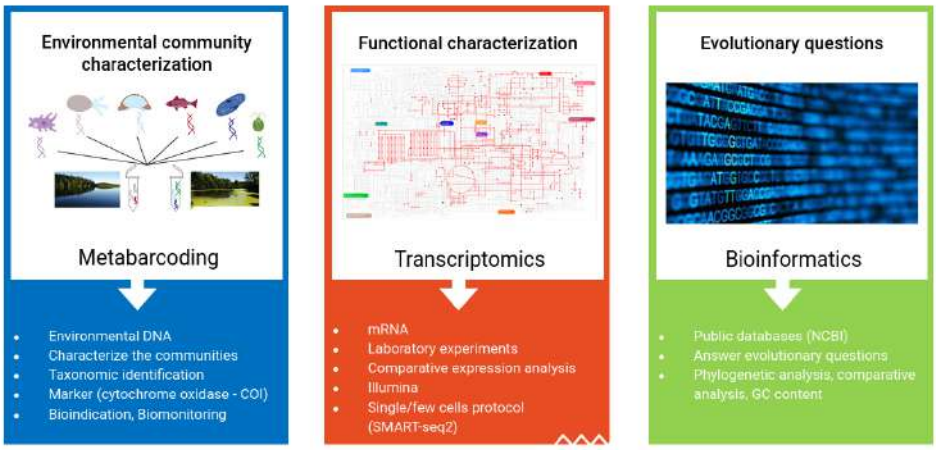
(ii) Characterize the molecular mechanism related to resistance;

(iii) Quantify gene expression in microcosms with different oxygenation levels;

(iv) Characterize expression patterns changes and the relevance of fermentative metabolism in the tolerance of arcellinids to low oxygen conditions.

1.11 Methods

Figura 11 – Methodological approaches that were applied in this thesis. (i) Metabarcoding: Describe the arcellinid communities in the conditions of interest - Appendix A; (ii) Transcriptomics: Functional characterization using mRNA sequencing and gene expression analysis - Chapters 4 and 6; (iii) Bioinformatics: Obtaining available data in public databases to answer evolutionary questions - Chapters 3 and 5.



1.11.1 Database expansion and species descriptions

The manuscript corresponding to the Chapter 2 of the thesis is complete and was submitted to the European Journal of Protistology. We decided to produce this initial manuscript because we need more precision in Arcellinida identification in our applied works. Previously, we named the "model"organisms used in our experiments with raw designations based on original species descriptions. However, although we always included the location where we took the cells, this caused a problem in the replicability of the experiments. The reason is that another investigator can take a cryptic species of the organism we used as a "model"and obtain different results because of lineage-specific differences. Currently, we have a practical and less subjective way to identify the amoebae, which is cytochrome oxidase (COI) barcoding. In that way, before publishing the next manuscripts of the project using our "model"species, we wanted to use barcoding, in conjunction with morphology and morphometry, to describe *Arcella uspiensis*, the

species we currently use as "model,"and other Arcellinida species that we had in the laboratory. Also, we used this manuscript to expand the COI database we use in Arcellinida identification adding transcriptomic data fished bioinformatically. For this expansion, we used public transcriptome data available at NCBI, data present in our laboratory database, and the production of new sequences through PCR and Sanger sequencing. We carried out this parallel analysis because although COI is the marker with more sequences available for arcellinids, the group's biodiversity is still underrepresented (GONZáLEZ-MIGUéNS et al., 2023). We applied this expanded database to identify taxonomic unities (OTUs) in the environmental study we presented in Appendix A.

1.11.2 Molecular evolution of resistance metabolism pathways

Previous studies have elucidated the mechanisms of resistance employed by organisms under low oxygen and arsenical stress conditions. The selection of relevant genes in this study was based on comprehensive reviews of the literature by Stairs et al. (2015) and Chen et al. (2020) (STAIRS; LEGER; ROGER, 2015; CHEN et al., 2020). A bioinformatical methodology, as described by Hofstatter et al. (2016), was employed to identify these genes from public databases and transcriptomes of Arcellinida (HOFSTATTER et al., 2016). Subsequently, gene trees were constructed to propose a hypothesis regarding the evolutionary relationships of these genes, as detailed in Chapters 3 and 5 of this document.

1.11.3 Functional characterization through transcriptomics

Previous ecological studies found Arcellinids species present under low oxygen and arsenic environmental pressures (ROE; PATTERSON; SWINDLES, 2010; ROE; PATTERSON, 2014; PATTERSON et al., 2019; DANIEL; LOPES, 2006; REGALADO et al., 2018; JU et al., 2014; KOSAKYAN; LARA, 2019; SILVA et al., 2013; ORTIZ et al., 2009; CZAPLUK; RUTKOWSKI; RYBAK, 2018). Also, through comparative analyses, we determined that Arcellinids had genes of resistance to arsenic and low oxygen (Chapters 4 and 6). In this second work front, we made laboratory-controlled experiments. We used *Arcella uspiensis* in the experiments, a species that we always use as a "model"in the laboratory. We chose *Arcella uspiensis* because this is the species that we have been able

to keep in cultivation since 2013, and we have the most information about basic biology, such as growth curves and metabolism (RIBEIRO et al., 2020; RIBEIRO et al., 2019; HOFSTATTER; LAHR, 2019; PORFÍRIO-SOUSA; RIBEIRO; LAHR, 2017). We also have a reference transcriptome built for the group, which we can use to map the produced transcriptome data (RIBEIRO et al., 2020). Thus, this experiment consisted of growing *Arcella uspiensis* cultures in controlled environments on both arsenic and low oxygen conditions. We followed the SMARTseq2 methodology for producing transcriptomes (PICELLI et al., 2014). In this methodology, we isolate one or a few cells from the culture, isolate the messenger RNA by bead selection, transform it into cDNA by reverse transcription, prepare the libraries, and sequence them by Illumina. The entire methodology for producing these transcriptomes and analyses is described in more detail in Chapters 4 and 6, where we show the results obtained in these experiments.

1.11.4 Characterization of the community in the environment through Metabarcoding

The rationale behind the metabarcoding technique is that each organism has unique portions of its DNA sequence that can identify them at the species level. In the work included in Appendix A, we compared the arcellinid community between urban lakes (within Madrid) and lakes outside the city, with less anthropic interference. We will describe the sampling points in more detail in Appendix A, where we describe the results of this experiment. With this sample, we performed DNA extractions and amplification of the cytochrome oxidase (COI) marker, currently the most used marker in testate amoebae identification (GONZáLEZ-MIGUéNS et al., 2023). We sequenced through the Novaseq platform.

1.12 Document structure

This thesis is organized into chapters containing an introduction (Chapter 1), the main manuscripts produced (Chapters 2, 3, 4, 5, and 6), a final discussion (Chapter 7), and an extra metabarcoding experiment still under analysis (Appendix A). In chapters 3 and 5, the manuscripts in which we characterize the presence and absence of resistance pathways in eukaryotes and arcellinids through Bioinformatics are published or submitted

to Molecular Phylogenetics and Evolution. In chapters 4 and 6, we described the gene expression results and will still prepare these chapters for publication. Finally, we still need to finish the analysis of Appendix A data, and we want to prepare the discussion chapter 7 to publish as an opinion article.

7.2 Final conclusion

Model organisms are useful because we put a lot of effort into building a basis of basic knowledge for this organism. After that, you can apply this knowledge to a wider range of organisms. *Arcella uspiensis* has great potential as a model organism in Arcellinida. We have already built up a lot of basic knowledge about this group (RIBEIRO et al., 2019; RIBEIRO et al., 2020; RIBEIRO; LAHR, 2022; PORFÍRIO-SOUSA; RIBEIRO; LAHR, 2017; LAHR et al., 2019; GONZáLEZ-MIGUéNS et al., 2023; GONZÁLEZ-MIGUÉNS et al., 2022b; GONZÁLEZ-MIGUÉNS et al., 2022a; HOFSTATTER et al., 2016). In this thesis, we developed two transcriptomic experiments in stressful conditions (low-oxygen and arsenic-contaminated). Also, we performed bioinformatic studies fishing genes of interest and building inferences about resistance evolution. In applied science, we started to develop primers for qPCR of resistance genes (Chapters 4 and 6). Also, we amplified COI database for Arcellinids and performed a metabarcoding study in Madrid.

Bibliography

ABE, T. et al. Anaerobic elemental sulfur reduction by fungus fusarium oxysporum. *Bioscience, biotechnology, and biochemistry*, Oxford University Press, v. 71, n. 10, p. 2402–2407, 2007. Citado na página 246.

ADJIRACKOR, N. A.; HARVEY, K. E.; HARVEY, S. C. Eukaryotic response to hypothermia in relation to integrated stress responses. *Cell Stress and Chaperones*, Springer, v. 25, p. 833–846, 2020. Citado na página 280.

ADL, S. M. et al. Revisions to the classification, nomenclature, and diversity of eukaryotes. *Journal of Eukaryotic Microbiology*, Wiley Online Library, v. 66, n. 1, p. 4–119, 2019. Citado 2 vezes nas páginas 104 e 106.

AGUILERA, A. et al. Distribution and seasonal variability in the benthic eukaryotic community of rio tinto (sw, spain), an acidic, high metal extreme environment. *Systematic and Applied Microbiology*, Elsevier, v. 30, n. 7, p. 531–546, 2007. Citado 3 vezes nas páginas 101, 137 e 282.

ALEXANDER, T. J.; VONLANTHEN, P.; SEEHAUSEN, O. Does eutrophication-driven evolution change aquatic ecosystems? *Philosophical Transactions of the Royal Society B: Biological Sciences*, The Royal Society, v. 372, n. 1712, p. 20160041, 2017. Citado 2 vezes nas páginas 53 e 325.

ALIKHANI, S.; NUMMI, P.; OJALA, A. Urban wetlands: A review on ecological and cultural values. *Water*, MDPI, v. 13, n. 22, p. 3301, 2021. Citado na página 324.

AMESBURY, M. J. et al. Towards a holarctic synthesis of peatland testate amoeba ecology: Development of a new continental-scale palaeohydrological transfer function for north america and comparison to european data. *Quaternary Science Reviews*, Elsevier, v. 201, p. 483–500, 2018. Citado na página 89.

ANDERSON, O. R. *Comparative protozoology: ecology, physiology, life history*. [S.l.]: Springer Science & Business Media, 2013. Citado na página 247.

ANDREEVA, A. V.; KUTUZOV, M. A. Protozoan protein tyrosine phosphatases. *International journal for parasitology*, Elsevier, v. 38, n. 11, p. 1279–1295, 2008. Citado 2 vezes nas páginas 108 e 115.

ANDREWS, S. et al. Fastqc: a quality control tool for high throughput sequence data. Babraham Bioinformatics, Babraham Institute, Cambridge, United Kingdom, 2010. Citado 3 vezes nas páginas 161, 249 e 328.

ANDREY, T.; YURI, M. Morphology and biometry of arcella intermedia (deflandre, 1928) comb. nov.. from russia and a review of hemispheric species of the genus arcella (testcealobosea, arcellinida). *Protistology*, ..., v. 4, n. 4, p. 361–369, 2006. Citado 2 vezes nas páginas 80 e 86.

ANI, J. U. et al. Abstraction of arsenic (iii) on activated carbon prepared from dialium guineense seed shell: kinetics, isotherms and thermodynamic studies. *SN Applied Sciences*, Springer, v. 1, p. 1–11, 2019. Citado na página 161.

ANNESLEY, S. J.; FISHER, P. R. Dictyostelium discoideum—a model for many reasons. *Molecular and cellular biochemistry*, Springer, v. 329, p. 73–91, 2009. Citado na página 38.

ANTIA, N.; BILINSKI, E.; LAU, Y. Identification and characterization of phospholipase d in a unicellular red alga (porphyridium cruentum). *Canadian journal of biochemistry*, NRC Research Press Ottawa, Canada, v. 48, n. 6, p. 643–648, 1970. Citado na página 195.

ANTÓNIO, C. et al. Regulation of primary metabolism in response to low oxygen availability as revealed by carbon and nitrogen isotope redistribution. *Plant Physiology*, American Society of Plant Biologists, v. 170, n. 1, p. 43–56, 2016. Citado na página 54.

ARGOS, M.; AHSAN, H.; GRAZIANO, J. H. Arsenic and human health: epidemiologic progress and public health implications. *Reviews on environmental health*, De Gruyter, v. 27, n. 4, p. 191–195, 2012. Citado na página 158.

ARRIEIRA, R. L. et al. Local factors affecting the testate amoeba community (protozoa: Arcellinida; euglyphida) in a neotropical floodplain. *Journal of Limnology*, Citeseer, v. 74, n. 3, 2015. Citado 3 vezes nas páginas 43, 62 e 325.

ATASIEI, D. et al. Impact of post-tropical storm arthur (2014) on benthic arcellinida assemblage dynamics in harvey lake, new brunswick, canada. *Hydrobiologia*, Springer, v. 849, n. 13, p. 3041–3059, 2022. Citado 3 vezes nas páginas 43, 62 e 325.

ATTEIA, A. et al. Pyruvate formate-lyase and a novel route of eukaryotic atp synthesis in chlamydomonas mitochondria. *Journal of Biological Chemistry*, ASBMB, v. 281, n. 15, p. 9909–9918, 2006. Citado 3 vezes nas páginas 196, 206 e 247.

BABCOCK, G. T. How oxygen is activated and reduced in respiration. *Proceedings of the National Academy of Sciences*, National Acad Sciences, v. 96, n. 23, p. 12971–12973, 1999. Citado na página 281.

BABKO, R. et al. Oxygen gradients and structure of the ciliate assemblages in floodplain lake. *Water*, MDPI, v. 12, n. 8, p. 2084, 2020. Citado na página 267.

BAESSOLO, L. First records and community pattern of arcellinida inhabiting a pristine and remote island from southeastern pacific, chile. *Acta Protozoologica*, Uniwersytet Jagielloński. Wydawnictwo Uniwersytetu Jagiellońskiego, v. 51, n. 2, 2012. Citado na página 83.

BAFFY, G. Mitochondrial uncoupling in cancer cells: Liabilities and opportunities. *Biochimica et Biophysica Acta (BBA)-Bioenergetics*, Elsevier, v. 1858, n. 8, p. 655–664, 2017. Citado na página 269.

BAILEY, T. L. et al. Meme suite: tools for motif discovery and searching. *Nucleic acids research*, Oxford University Press, v. 37, n. suppl_2, p. W202–W208, 2009. Citado na página 105.

BALDAUF, S. L.; DOOLITTLE, W. F. Origin and evolution of the slime molds (mycetozoa). *Proceedings of the National Academy of Sciences*, National Acad Sciences, v. 94, n. 22, p. 12007–12012, 1997. Citado na página 36.

BARRA, C. M. et al. Especiação de arsênio-uma revisão. *Química Nova*, SciELO Brasil, v. 23, n. 1, p. 58–70, 2000. Citado 3 vezes nas páginas 47, 48 e 158.

BAUCHOP, T. Biology of gut anaerobic fungi. *Biosystems*, Elsevier, v. 23, n. 1, p. 53–64, 1989. Citado na página 243.

BAUMGARTNER, M. et al. Cultivation and properties of echinamoeba thermarum n. sp., an extremely thermophilic amoeba thriving in hot springs. *Extremophiles*, Springer, v. 7, p. 267–274, 2003. Citado na página 69.

BENOISTON, A.-S. et al. The evolution of diatoms and their biogeochemical functions. *Philosophical Transactions of the Royal Society B: Biological Sciences*, The Royal Society, v. 372, n. 1728, p. 20160397, 2017. Citado na página 36.

BENTLEY, R.; CHASTEEN, T. G. Microbial methylation of metalloids: arsenic, antimony, and bismuth. *Microbiology and molecular biology reviews*, Am Soc Microbiol, v. 66, n. 2, p. 250–271, 2002. Citado na página 138.

BERNARD, C.; FENCHEL, T. Some microaerobic ciliates are facultative anaerobes. *European Journal of Protistology*, Elsevier, v. 32, n. 3, p. 293–297, 1996. Citado na página 243.

BERNHARDT, J. R. et al. Life in fluctuating environments. *Philosophical Transactions of the Royal Society B*, The Royal Society, v. 375, n. 1814, p. 20190454, 2020. Citado na página 280.

BERNSTEIN, H.; BERNSTEIN, C. Evolutionary origin of recombination during meiosis. *BioScience*, American Institute of Biological Sciences Circulation, AIBS, 1313 Dolley ..., v. 60, n. 7, p. 498–505, 2010. Citado 2 vezes nas páginas 200 e 286.

BHATTACHARJEE, H.; ROSEN, B. P. Arsenic metabolism in prokaryotic and eukaryotic microbes. In: *Molecular microbiology of heavy metals*. [S.l.]: Springer, 2007. p. 371–406. Citado 3 vezes nas páginas 49, 99 e 159.

BLANDENIER, Q. et al. Nad9/nad7 (mitochondrial nicotinamide adenine dinucleotide dehydrogenase gene)—a new "holy grail" phylogenetic and dna-barcoding marker for arcellinida (amoebozoa)? *European Journal of Protistology*, Elsevier, v. 58, p. 175–186, 2017. Citado 2 vezes nas páginas 64 e 326.

BLAXTER, M. et al. Why sequence all eukaryotes? *Proceedings of the National Academy of Sciences*, National Acad Sciences, v. 119, n. 4, p. e2115636118, 2022. Citado na página 44.

BOBROV, A.; MAZEI, Y. Morphological variability of testate amoebae (rhizopoda: Testacealobosea and testaceafilosea) in natural populations. *Acta Protozoologica*, POLISH ACADEMY OF SCIENCES, v. 43, n. 2, p. 133–146, 2004. Citado na página 63.

BOLGER, A. M.; LOHSE, M.; USADEL, B. Trimmomatic: a flexible trimmer for illumina sequence data. *Bioinformatics*, Oxford University Press, v. 30, n. 15, p. 2114–2120, 2014. Citado 4 vezes nas páginas 162, 207, 209 e 249.

BOOTMAN, M. D. et al. Calcium signalling and regulation of cell function. *eLS*, John Wiley & Sons, Ltd, 2012. Citado na página 195.

BORDO, D.; BORK, P. The rhodanese/cdc25 phosphatase superfamily. *EMBO reports*, John Wiley & Sons, Ltd, v. 3, n. 8, p. 741–746, 2002. Citado 2 vezes nas páginas 108 e 134.

BOTTINO, N. et al. The effects of arsenate and arsenite on the growth and morphology of the marine unicellular algae tetraselmis chui (chlorophyta) and hymenomonas carterae (chrysophyta). *Journal of Experimental Marine Biology and Ecology*, Elsevier, v. 33, n. 2, p. 153–168, 1978. Citado na página 195.

BOXMA, B. et al. An anaerobic mitochondrion that produces hydrogen. *Nature*, Nature Publishing Group, v. 434, n. 7029, p. 74, 2005. Citado 2 vezes nas páginas 227 e 273.

BRAAK, C. J. T.; VERDONSCHOT, P. F. Canonical correspondence analysis and related multivariate methods in aquatic ecology. *Aquatic sciences*, Springer, v. 57, p. 255–289, 1995. Citado na página 329.

BROWN, M. W.; SPIEGEL, F. W.; SILBERMAN, J. D. Phylogeny of the "forgotten" cellular slime mold, fonticula alba, reveals a key evolutionary branch within opisthokonta. *Molecular Biology and Evolution*, Oxford University Press, v. 26, n. 12, p. 2699–2709, 2009. Citado na página 36.

BURDMAN, L. et al. A reassessment of testate amoebae diversity in tierra del fuego peatlands: Implications for large scale inferences. *European Journal of Protistology*, Elsevier, v. 80, p. 125806, 2021. Citado na página 81.

BURKI, F. et al. The new tree of eukaryotes. *Trends in ecology & evolution*, Elsevier, v. 35, n. 1, p. 43–55, 2020. Citado 8 vezes nas páginas 7, 13, 36, 37, 42, 104, 106 e 110.

CALISI, R. M.; BENTLEY, G. E. Lab and field experiments: are they the same animal? *Hormones and behavior*, Elsevier, v. 56, n. 1, p. 1–10, 2009. Citado na página 285.

CALLAHAN, B. J. et al. Dada2: High-resolution sample inference from illumina amplicon data. *Nature methods*, Nature Publishing Group US New York, v. 13, n. 7, p. 581–583, 2016. Citado na página 328.

CÁNOVAS, D. et al. Testing the limits of biological tolerance to arsenic in a fungus isolated from the river tinto. *Environmental Microbiology*, Wiley Online Library, v. 5, n. 2, p. 133–138, 2003. Citado na página 195.

CAPELLA-GUTIÉRREZ, S.; SILLA-MARTÍNEZ, J. M.; GABALDÓN, T. trimal: a tool for automated alignment trimming in large-scale phylogenetic analyses. *Bioinformatics*, Oxford University Press, v. 25, n. 15, p. 1972–1973, 2009. Citado 3 vezes nas páginas 68, 104 e 209.

CARVALHO, M. S. de et al. Concentração de metais no rio doce em mariana, minas gerais, brasil. *Acta Brasiliensis*, v. 1, n. 3, p. 37–41, 2017. Citado na página 46.

CASTILLO, R.; SAIER, M. H. Functional promiscuity of homologues of the bacterial arsa atpases. *International journal of microbiology*, Hindawi Publishing Corporation, v. 2010, 2010. Citado na página 111.

CASTRESANA, J. Topological variation in single-gene phylogenetic trees. *Genome biology*, BioMed Central, v. 8, n. 6, p. 216, 2007. Citado 2 vezes nas páginas 225 e 226.

CATALANOTTI, C. et al. Fermentation metabolism and its evolution in algae. *Frontiers in plant science*, Frontiers Media SA, v. 4, 2013. Citado 11 vezes nas páginas 53, 54, 205, 224, 226, 227, 243, 273, 274, 276 e 283.

CELEWICZ, S.; GOŁDYN, B. Phytoplankton communities in temporary ponds under different climate scenarios. *Scientific Reports*, Springer, v. 11, n. 1, p. 1–15, 2021. Citado na página 286.

CHANDEL, N. S. Signaling and metabolism. *Cold Spring Harbor Perspectives in Biology*, Cold Spring Harbor Lab, v. 13, n. 2, p. a040600, 2021. Citado na página 244.

CHARDEZ, D. Difflugia oblonga ehrenberg et ses varietes. *Bull. Inst. Agron. Stat. Rech. Gembloux, new series*, v. 2, n. 4, p. 589–595, 1967. Citado na página 40.

CHAUDHRY, R.; VARACALLO, M. Biochemistry, glycolysis. 2018. Citado 2 vezes nas páginas 244 e 271.

CHEN, J.; BHATTACHARJEE, H.; ROSEN, B. P. Arsh is an organoarsenical oxidase that confers resistance to trivalent forms of the herbicide msma and the poultry growth promoter roxarsone. *Molecular microbiology*, NIH Public Access, v. 96, n. 5, p. 1042, 2015. Citado 2 vezes nas páginas 100 e 130.

CHEN, J. et al. Arsp: a methylarsenite efflux permease. *Molecular microbiology*, Wiley Online Library, v. 98, n. 4, p. 625–635, 2015. Citado na página 100.

CHEN, J.; ROSEN, B. P. The arsenic methylation cycle: how microbial communities adapted methylarsenicals for use as weapons in the continuing war for dominance. *Frontiers in Environmental Science*, Frontiers Research Foundation, 2020. Citado 4 vezes nas páginas 99, 158, 281 e 282.

CHEN, J.; YOSHINAGA, M.; ROSEN, B. P. The antibiotic action of methylarsenite is an emergent property of microbial communities. *Molecular microbiology*, Wiley Online Library, v. 111, n. 2, p. 487–494, 2019. Citado na página 159.

CHEN, S.-C. et al. Recurrent horizontal transfer of arsenite methyltransferase genes facilitated adaptation of life to arsenic. *Scientific reports*, Nature Publishing Group, v. 7, n. 1, p. 1–11, 2017. Citado 4 vezes nas páginas 102, 120, 132 e 133.

CHEN, S.-C. et al. The great oxidation event expanded the genetic repertoire of arsenic metabolism and cycling. *Proceedings of the National Academy of Sciences*, National Acad Sciences, v. 117, n. 19, p. 10414–10421, 2020. Citado 15 vezes nas páginas 12, 47, 48, 49, 50, 58, 98, 99, 101, 108, 133, 140, 159, 281 e 282.

CHEN, Y. et al. Arsenic transport in rice and biological solutions to reduce arsenic risk from rice. *Frontiers in plant science*, Frontiers, v. 8, p. 268, 2017. Citado na página 102.

CHOURPILIADIS, C.; MOHIUDDIN, S. S. Biochemistry, gluconeogenesis. 2019. Citado na página 244.

CLAROS, M. G. Mitoprot, a macintosh application for studying mitochondrial proteins. *Bioinformatics*, Oxford University Press, v. 11, n. 4, p. 441–447, 1995. Citado na página 208.

COCHET-ESCARTIN, O. et al. Hypoxia triggers collective aerotactic migration in dictyostelium discoideum. *Elife*, eLife Sciences Publications Limited, v. 10, p. e64731, 2021. Citado na página 280.

COLLINS, F. S.; MCKUSICK, V. A. Implications of the human genome project for medical science. *Jama*, American Medical Association, v. 285, n. 5, p. 540–544, 2001. Citado na página 37.

CONESA, A. et al. Blast2go: a universal tool for annotation, visualization and analysis in functional genomics research. *Bioinformatics*, Oxford University Press, v. 21, n. 18, p. 3674–3676, 2005. Citado 3 vezes nas páginas 106, 162 e 250.

COOPER, C. et al. Mitochondrial superoxide and aging: uncoupling-protein activity and superoxide production. In: PORTLAND PRESS. *Biochemical Society Symposia*. [S.l.], 2004. v. 71, p. 203–213. Citado na página 269.

COTE-L'HEUREUX, A.; MAURER-ALCALÁ, X. X.; KATZ, L. A. Old genes in new places: a taxon-rich analysis of interdomain lateral gene transfer events. *PLoS genetics*, Public Library of Science San Francisco, CA USA, v. 18, n. 6, p. e1010239, 2022. Citado na página 208.

COWMAN, A. F. et al. Malaria: biology and disease. *Cell*, Elsevier, v. 167, n. 3, p. 610–624, 2016. Citado na página 36.

CROWTHER, T. W.; BODDY, L.; JONES, H. T. Functional and ecological consequences of saprotrophic fungus–grazer interactions. *The ISME journal*, Nature Publishing Group, v. 6, n. 11, p. 1992–2001, 2012. Citado na página 39.

CRUTZEN, P. J.; STOERMER, E. F. *The 'anthropocene'(2000)*. [S.l.]: Springer, 2021. Citado na página 40.

CZAPLUK, B.; RUTKOWSKI, R.; RYBAK, J. Microfauna composition of activated sludge in domestic and industrial sewage activated sludge systems. *Environment Protection Engineering*, v. 44, n. 1, 2018. Citado 2 vezes nas páginas 43 e 58.

DANIEL, J.; LOPES, S. G. Morphology, biometry, ecology and biogeography of five species of difflugia leclerc, 1815 (arcellinida: Difflugiidae), from tiete river, brazil. *Acta Protozool*, Citeseer, v. 45, p. 77–90, 2006. Citado 2 vezes nas páginas 43 e 58.

DHANKHER, O. P. et al. Hyperaccumulation of arsenic in the shoots of arabidopsis silenced for arsenate reductase (acr2). *Proceedings of the National Academy of Sciences*, National Acad Sciences, v. 103, n. 14, p. 5413–5418, 2006. Citado na página 134.

DIETRICH, M. R.; ANKENY, R. A.; CHEN, P. M. Publication trends in model organism research. *Genetics*, Oxford University Press, v. 198, n. 3, p. 787–794, 2014. Citado na página 37.

DIJKEN, J. P. van; SCHEFFERS, W. A. Redox balances in the metabolism of sugars by yeasts. *FEMS microbiology letters*, Elsevier, v. 32, n. 3-4, p. 199–224, 1986. Citado 2 vezes nas páginas 226 e 276.

DING, W. et al. Inhibition of poly (adp-ribose) polymerase-1 by arsenite interferes with repair of oxidative dna damage. *Journal of Biological Chemistry*, ASBMB, v. 284, n. 11, p. 6809–6817, 2009. Citado 3 vezes nas páginas 49, 159 e 281.

DIXON, H. B. The biochemical action of arsonic acids especially as phosphate analogues. In: *Advances in inorganic chemistry*. [S.l.]: Elsevier, 1996. v. 44, p. 191–227. Citado na página 198.

DONKER, L. et al. A mechanical g2 checkpoint controls epithelial cell division through e-cadherin-mediated regulation of wee1-cdk1. *Cell Reports*, Elsevier, v. 41, n. 2, p. 111475, 2022. Citado na página 200.

DUAN, G.-L. et al. A cdc25 homologue from rice functions as an arsenate reductase. *New Phytologist*, Wiley Online Library, v. 174, n. 2, p. 311–321, 2007. Citado na página 134.

DUCKERT, C. et al. En garde! redefinition of nebela militaris (arcellinida, hyalospheniidae) and erection of alabasta gen. nov. *European journal of Protistology*, Elsevier, v. 66, p. 156–165, 2018. Citado 2 vezes nas páginas 66 e 68.

DUMACK, K. et al. Reinvestigation of phryganella paradoxa (arcellinida, amoebozoa) penard 1902. *Journal of Eukaryotic Microbiology*, Wiley Online Library, v. 66, n. 2, p. 232–243, 2019. Citado na página 67.

DUNCAN, E. G.; MAHER, W. A.; FOSTER, S. D. Contribution of arsenic species in unicellular algae to the cycling of arsenic in marine ecosystems. *Environmental science & technology*, ACS Publications, v. 49, n. 1, p. 33–50, 2015. Citado na página 137.

EHREBERG, C. Die infusionsthierchen als vollkommene organismen. *Leopold Voss, Leipzig, Germany*, 1838. Citado 2 vezes nas páginas 69 e 89.

EHRENBERG, C. Überdieentwickelungundlebensdauerder infusionsthiere. abhandl. k. *Akad. Wissensch. Berlin*, p. 1–154, 1831. Citado na página 280.

ELLIS, D. R. et al. A novel arsenate reductase from the arsenic hyperaccumulating fern pteris vittata. *Plant physiology*, Am Soc Plant Biol, v. 141, n. 4, p. 1544–1554, 2006. Citado na página 134.

EMANUELSSON, O. et al. Locating proteins in the cell using targetp, signalp and related tools. *Nature protocols*, Nature Publishing Group, v. 2, n. 4, p. 953, 2007. Citado na página 208.

EME, L. et al. Lateral gene transfer in the adaptation of the anaerobic parasite blastocystis to the gut. *Current Biology*, Elsevier, v. 27, n. 6, p. 807–820, 2017. Citado na página 138.

EME, L. et al. On the age of eukaryotes: evaluating evidence from fossils and molecular clocks. *Cold Spring Harbor Perspectives in Biology*, Cold Spring Harbor Lab, v. 6, n. 8, p. a016139, 2014. Citado na página 140.

FACCIO, G. et al. Sulfhydryl oxidases: sources, properties, production and applications. *Applied microbiology and biotechnology*, Springer, v. 91, p. 957–966, 2011. Citado 2 vezes nas páginas 178 e 199.

FAHIE, K. M.; PAPANICOLAOU, K. N.; ZACHARA, N. E. Integration of o-glcnac into stress response pathways. *Cells*, MDPI, v. 11, n. 21, p. 3509, 2022. Citado na página 199.

FAITA, F. et al. Arsenic-induced genotoxicity and genetic susceptibility to arsenic-related pathologies. *International journal of environmental research and public health*, MDPI, v. 10, n. 4, p. 1527–1546, 2013. Citado na página 158.

FEKIH, I. B. et al. Distribution of arsenic resistance genes in prokaryotes. *Frontiers in microbiology*, Frontiers, v. 9, p. 2473, 2018. Citado 2 vezes nas páginas 49 e 99.

FENCHEL, T. Microbial behavior in a heterogeneous world. *Science*, American Association for the Advancement of Science, v. 296, n. 5570, p. 1068–1071, 2002. Citado na página 280.

FENCHEL, T. Anaerobic eukaryotes. In: *Anoxia*. [S.l.]: Springer, 2012. p. 3–16. Citado 2 vezes nas páginas 243 e 283.

FENCHEL, T.; FINLAY, B. J. The ubiquity of small species: patterns of local and global diversity. *Bioscience*, American Institute of Biological Sciences, v. 54, n. 8, p. 777–784, 2004. Citado na página 286.

FENG, Y. et al. Comparative genomics reveals insight into the evolutionary origin of massively scrambled genomes. *Elife*, eLife Sciences Publications Limited, v. 11, p. e82979, 2022. Citado na página 44.

FERGUSON, J. F.; GAVIS, J. A review of the arsenic cycle in natural waters. *Water research*, Elsevier, v. 6, n. 11, p. 1259–1274, 1972. Citado na página 140.

FIELD, C. B. et al. Primary production of the biosphere: integrating terrestrial and oceanic components. *science*, American Association for the Advancement of Science, v. 281, n. 5374, p. 237–240, 1998. Citado na página 36.

FINN, R. D.; CLEMENTS, J.; EDDY, S. R. Hmmer web server: interactive sequence similarity searching. *Nucleic acids research*, Oxford University Press, v. 39, n. suppl_2, p. W29–W37, 2011. Citado 2 vezes nas páginas 68 e 104.

FIORE-DONNO, A. M. et al. Deep phylogeny and evolution of slime moulds (mycetozoa). *Protist*, Elsevier, v. 161, n. 1, p. 55–70, 2010. Citado na página 36.

FISI, V.; MISETA, A.; NAGY, T. The role of stress-induced o-glcnac protein modification in the regulation of membrane transport. *Oxidative Medicine and Cellular Longevity*, Hindawi, v. 2017, 2017. Citado na página 199.

FIZ-PALACIOS, O.; LEANDER, B. S.; HEGER, T. J. Old lineages in a new ecosystem: diversification of arcellinid amoebae (amoebozoa) and peatland mosses. *PLoS One*, Public Library of Science San Francisco, USA, v. 9, n. 4, p. e95238, 2014. Citado na página 344.

FLORA, S. J. Arsenic-induced oxidative stress and its reversibility. *Free Radical Biology and Medicine*, Elsevier, v. 51, n. 2, p. 257–281, 2011. Citado 5 vezes nas páginas 49, 99, 158, 159 e 281.

FLOREA, A.-M.; YAMOAH, E. N.; DOPP, E. Intracellular calcium disturbances induced by arsenic and its methylated derivatives in relation to genomic damage and apoptosis induction. *Environmental health perspectives*, National Institue of Environmental Health Sciences, v. 113, n. 6, p. 659–664, 2005. Citado na página 195.

FOISSNER, W. Protist diversity and distribution: some basic considerations. *Protist diversity and geographical distribution*, Springer, p. 1–8, 2009. Citado na página 286.

FOLMER, O. et al. *DNA primers for amplification of mitochondrial cytochrome c oxidase subunit I from diverse metazoan invertebrates 3, 294–299*. 1994. Citado 2 vezes nas páginas 66 e 328.

FOURNIER, A. The story of symbiosis with zooxanthellae, or how they enable their host to thrive in a nutrient poor environment. *Master Biosci Rev-Ec Norm Supérieure Lyon*, v. 8, 2013. Citado na página 36.

FRANCISCO, P. D. et al. Interactions with arsenic: Mechanisms of toxicity and cellular resistance in eukaryotic microorganisms. *International journal of environmental research and public health*, Multidisciplinary Digital Publishing Institute, v. 18, n. 22, p. 12226, 2021. Citado na página 160.

FRITZ-LAYLIN, L. K. et al. The genome of naegleria gruberi illuminates early eukaryotic versatility. *Cell*, Elsevier, v. 140, n. 5, p. 631–642, 2010. Citado 3 vezes nas páginas 205, 206 e 283.

FRU, E. C. et al. Arsenic stress after the proterozoic glaciations. *Scientific reports*, Nature Publishing Group, v. 5, n. 1, p. 1–12, 2015. Citado 5 vezes nas páginas 98, 133, 140, 281 e 282.

FRU, E. C. et al. The rise of oxygen-driven arsenic cycling at ca. 2.48 ga. *Geology*, GeoScienceWorld, v. 47, n. 3, p. 243–246, 2019. Citado 4 vezes nas páginas 98, 99, 281 e 282.

GABALDÓN, T.; MARCET-HOUBEN, M. 3 phylogenomics for the study of fungal biology. In: *Fungal Genomics*. [S.l.]: Springer, 2014. p. 61–79. Citado na página 132.

GALLOWAY, J. M. et al. Organic matter control on the distribution of arsenic in lake sediments impacted by˜ 65 years of gold ore processing in subarctic canada. *Science of the Total Environment*, Elsevier, v. 622, p. 1668–1679, 2018. Citado na página 46.

GARCÍA-SALGADO, S. et al. Arsenosugar phospholipids and arsenic hydrocarbons in two species of brown macroalgae. *Environmental Chemistry*, CSIRO, v. 9, n. 1, p. 63–66, 2012. Citado na página 137.

GAWRYLUK, R. M. et al. The earliest stages of mitochondrial adaptation to low oxygen revealed in a novel rhizarian. *Current Biology*, Elsevier, v. 26, n. 20, p. 2729–2738, 2016. Citado 3 vezes nas páginas 205, 213 e 226.

GHOSH, M.; SHEN, J.; ROSEN, B. P. Pathways of as (iii) detoxification in saccharomyces cerevisiae. *Proceedings of the National Academy of Sciences*, National Acad Sciences, v. 96, n. 9, p. 5001–5006, 1999. Citado 2 vezes nas páginas 50 e 159.

GILL, E. E. et al. Novel mitochondrion-related organelles in the anaerobic amoeba mastigamoeba balamuthi. *Molecular microbiology*, Wiley Online Library, v. 66, n. 6, p. 1306–1320, 2007. Citado 2 vezes nas páginas 205 e 283.

GINGER, M. L. et al. Intermediary metabolism in protists: a sequence-based view of facultative anaerobic metabolism in evolutionarily diverse eukaryotes. *Protist*, Elsevier, v. 161, n. 5, p. 642–671, 2010. Citado na página 243.

GISIN, J. et al. A rhodobacter capsulatus member of a universal permease family imports molybdate and other oxyanions. *Journal of bacteriology*, Am Soc Microbiol, v. 192, n. 22, p. 5943–5952, 2010. Citado 2 vezes nas páginas 108 e 109.

GOMAA, F. et al. One alga to rule them all: unrelated mixotrophic testate amoebae (amoebozoa, rhizaria and stramenopiles) share the same symbiont (trebouxiophyceae). *Protist*, Elsevier, v. 165, n. 2, p. 161–176, 2014. Citado na página 82.

GOMAA, F. et al. Ssu rrna phylogeny of arcellinida (amoebozoa) reveals that the largest arcellinid genus, difflugia leclerc 1815, is not monophyletic. *Protist*, Elsevier, v. 163, n. 3, p. 389–399, 2012. Citado na página 82.

GOMAA, F. et al. Morphological and molecular diversification of asian endemic difflugia tuberspinifera (amoebozoa, arcellinida): a case of fast morphological evolution in protists? *Protist*, Elsevier, v. 166, n. 1, p. 122–130, 2015. Citado na página 82.

GONZÁLEZ-MIGUÉNS, R. et al. Multiple convergences in the evolutionary history of the testate amoeba family arcellidae (amoebozoa: Arcellinida: Sphaerothecina): when the ecology rules the morphology. *Zoological Journal of the Linnean Society*, Oxford University Press UK, v. 194, n. 4, p. 1044–1071, 2022. Citado 7 vezes nas páginas 63, 64, 68, 80, 82, 289 e 326.

GONZÁLEZ-MIGUÉNS, R. et al. Deconstructing difflugia: The tangled evolution of lobose testate amoebae shells (amoebozoa: Arcellinida) illustrates the importance of convergent evolution in protist phylogeny. *Molecular Phylogenetics and Evolution*, Elsevier, v. 175, p. 107557, 2022. Citado 13 vezes nas páginas 7, 41, 42, 62, 63, 64, 68, 78, 81, 82, 289, 325 e 326.

GONZáLEZ-MIGUéNS, R. et al. A needle in a haystack: A new metabarcoding approach to survey diversity at the species level of arcellinida (amoebozoa: Tubulinea). *Molecular Ecology Resources*, v. 23, n. 5, p. 1034–1049, 2023. Disponível em: ⟨https://onlinelibrary.wiley.com/doi/abs/10.1111/1755-0998.13771⟩. Citado 15 vezes nas páginas 44, 58, 59, 64, 65, 66, 68, 75, 80, 81, 82, 288, 289, 326 e 328.

GOTO, T. et al. Wee1 inhibition enhances sensitivity to hypoxia/reoxygenation in hela cells. *Journal of Radiation Research*, Oxford University Press, v. 60, n. 5, p. 709–713, 2019. Citado na página 200.

GOUY, M.; GUINDON, S.; GASCUEL, O. Seaview version 4: a multiplatform graphical user interface for sequence alignment and phylogenetic tree building. *Molecular biology and evolution*, Oxford University Press, v. 27, n. 2, p. 221–224, 2010. Citado 2 vezes nas páginas 67 e 209.

GRABHERR, M. G. et al. Full-length transcriptome assembly from rna-seq data without a reference genome. *Nature biotechnology*, Nature Publishing Group US New York, v. 29, n. 7, p. 644–652, 2011. Citado 4 vezes nas páginas 161, 207, 209 e 249.

GRANT, J. R.; KATZ, L. A. Phylogenomic study indicates widespread lateral gene transfer in entamoeba and suggests a past intimate relationship with parabasalids. *Genome biology and evolution*, Oxford University Press, v. 6, n. 9, p. 2350–2360, 2014. Citado na página 226.

GRINSVEN, K. W. van et al. Acetate: succinate coa-transferase in the hydrogenosomes of trichomonas vaginalis: identification and characterization. *Journal of Biological Chemistry*, ASBMB, v. 283, n. 3, p. 1411–1418, 2008. Citado 2 vezes nas páginas 210 e 226.

GU, C.; JUN, J. C. Does hypoxia decrease the metabolic rate? *Frontiers in Endocrinology*, Frontiers Media SA, v. 9, p. 668, 2018. Citado na página 246.

GUERRA, F. et al. Modulation of rab7a protein expression determines resistance to cisplatin through late endocytic pathway impairment and extracellular vesicular secretion. *Cancers*, MDPI, v. 11, n. 1, p. 52, 2019. Citado na página 186.

HALE, S. S.; CICCHETTI, G.; DEACUTIS, C. F. Eutrophication and hypoxia diminish ecosystem functions of benthic communities in a new england estuary. *Frontiers in Marine Science*, Frontiers Media SA, v. 3, p. 249, 2016. Citado 2 vezes nas páginas 53 e 325.

HALTER, D. et al. Arsenic hypertolerance in the protist euglena mutabilis is mediated by specific transporters and functional integrity maintenance mechanisms. *Environmental Microbiology*, Wiley Online Library, v. 17, n. 6, p. 1941–1949, 2015. Citado 5 vezes nas páginas 49, 159, 160, 196 e 281.

HAMPL, V.; STAIRS, C. W.; ROGER, A. J. The tangled past of eukaryotic enzymes involved in anaerobic metabolism. *Mobile genetic elements*, Taylor & Francis, v. 1, n. 1, p. 71–74, 2011. Citado na página 207.

HAN, Z.-J. et al. Oxidative stress is implicated in arsenic-induced neural tube defects in chick embryos. *International Journal of Developmental Neuroscience*, Elsevier, v. 29, n. 7, p. 673–680, 2011. Citado na página 197.

HAPPE, T. et al. Hydrogenases in green algae: do they save the algae's life and solve our energy problems? *Trends in plant science*, Elsevier, v. 7, n. 6, p. 246–250, 2002. Citado na página 277.

HASEGAWA, H. et al. Effect of eutrophication on the distribution of arsenic species in eutrophic and mesotrophic lakes. *Science of the Total Environment*, Elsevier, v. 407, n. 4, p. 1418–1425, 2009. Citado na página 46.

HASSALL, C. The ecology and biodiversity of urban ponds. *Wiley Interdisciplinary Reviews: Water*, Wiley Online Library, v. 1, n. 2, p. 187–206, 2014. Citado na página 324.

HECKMAN, C. W. *The Pantanal of Poconé: Biota and ecology in the northern section of the world's largest pristine wetland*. [S.l.]: Springer Science & Business Media, 2013. v. 77. Citado na página 275.

HEGER, T. J.; MITCHELL, E. A.; LEANDER, B. S. Holarctic phylogeography of the testate amoeba h yalosphenia papilio (amoebozoa: Arcellinida) reveals extensive genetic diversity explained more by environment than dispersal limitation. *Molecular ecology*, Wiley Online Library, v. 22, n. 20, p. 5172–5184, 2013. Citado 2 vezes nas páginas 62 e 325.

HEGER, T. J. et al. The curse of taxonomic uncertainty in biogeographical studies of free-living terrestrial protists: a case study of testate amoebae from amsterdam island. *Journal of biogeography*, Wiley Online Library, v. 36, n. 8, p. 1551–1560, 2009. Citado na página 285.

HENDRICK, H. M. et al. Phosphorylation of eukaryotic initiation factor-2θ during stress and encystation in entamoeba species. *PLoS pathogens*, Public Library of Science San Francisco, CA USA, v. 12, n. 12, p. e1006085, 2016. Citado na página 280.

HILLMANN, F. et al. Multiple roots of fruiting body formation in amoebozoa. *Genome biology and evolution*, Oxford University Press, v. 10, n. 2, p. 591–606, 2018. Citado na página 225.

HIROOKA, S. et al. Acidophilic green algal genome provides insights into adaptation to an acidic environment. *Proceedings of the National Academy of Sciences*, National Acad Sciences, v. 114, n. 39, p. E8304–E8313, 2017. Citado 2 vezes nas páginas 102 e 133.

HOFFMEISTER, M. et al. Euglena gracilis rhodoquinone: ubiquinone ratio and mitochondrial proteome differ under aerobic and anaerobic conditions. *Journal of Biological Chemistry*, ASBMB, v. 279, n. 21, p. 22422–22429, 2004. Citado 2 vezes nas páginas 196 e 197.

HOFSTATTER, P. G.; BROWN, M. W.; LAHR, D. J. Comparative genomics supports sex and meiosis in diverse amoebozoa. *Genome Biology and Evolution*, Oxford University Press, v. 10, n. 11, p. 3118–3128, 2018. Citado na página 201.

HOFSTATTER, P. G.; LAHR, D. J. All eukaryotes are sexual, unless proven otherwise: Many so-called asexuals present meiotic machinery and might be able to have sex. *BioEssays*, Wiley Online Library, v. 41, n. 6, p. 1800246, 2019. Citado 2 vezes nas páginas 45 e 59.

HOFSTATTER, P. G. et al. Evolution of bacterial recombinase a (reca) in eukaryotes explained by addition of genomic data of key microbial lineages. *Proceedings of the Royal Society B: Biological Sciences*, The Royal Society, v. 283, n. 1840, p. 20161453, 2016. Citado 3 vezes nas páginas 45, 58 e 289.

HOJSAK, I. et al. Arsenic in rice: a cause for concern. *Journal of pediatric gastroenterology and nutrition*, LWW, v. 60, n. 1, p. 142–145, 2015. Citado na página 159.

HÖRANDL, E.; HADACEK, F. The oxidative damage initiation hypothesis for meiosis. *Plant reproduction*, Springer, v. 26, p. 351–367, 2013. Citado 2 vezes nas páginas 200 e 286.

HORNER, D. S.; FOSTER, P. G.; EMBLEY, T. M. Iron hydrogenases and the evolution of anaerobic eukaryotes. *Molecular Biology and Evolution*, Oxford University Press, v. 17, n. 11, p. 1695–1709, 2000. Citado 2 vezes nas páginas 206 e 247.

HSU, W. et al. Differential effects of arsenic on calcium signaling in primary keratinocytes and malignant (hsc-1) cells. *Cell calcium*, Elsevier, v. 52, n. 2, p. 161–169, 2012. Citado na página 195.

HU, Y. et al. The role of reactive oxygen species in arsenic toxicity. *Biomolecules*, MDPI, v. 10, n. 2, p. 240, 2020. Citado na página 158.

HUG, L. A.; STECHMANN, A.; ROGER, A. J. Phylogenetic distributions and histories of proteins involved in anaerobic pyruvate metabolism in eukaryotes. *Molecular biology and evolution*, Oxford University Press, v. 27, n. 2, p. 311–324, 2009. Citado 2 vezes nas páginas 206 e 224.

HWANG, J.-H. et al. Modulation of energy metabolism is important for low-oxygen stress adaptation in brassicaceae species. *International Journal of Molecular Sciences*, MDPI, v. 21, n. 5, p. 1787, 2020. Citado na página 54.

IRION, U.; NÜSSLEIN-VOLHARD, C. Developmental genetics with model organisms. *Proceedings of the National Academy of Sciences*, National Acad Sciences, v. 119, n. 30, p. e2122148119, 2022. Citado na página 37.

JACOBSON, T. et al. Arsenite interferes with protein folding and triggers formation of protein aggregates in yeast. *Journal of cell science*, The Company of Biologists Ltd, v. 125, n. 21, p. 5073–5083, 2012. Citado 5 vezes nas páginas 49, 99, 159, 199 e 281.

JAGANNATHAN, L.; CUDDAPAH, S.; COSTA, M. Oxidative stress under ambient and physiological oxygen tension in tissue culture. *Current pharmacology reports*, Springer, v. 2, p. 64–72, 2016. Citado na página 267.

JENSEN, M. V. et al. Metabolic cycling in control of glucose-stimulated insulin secretion. *American Journal of Physiology-Endocrinology and Metabolism*, American Physiological Society, v. 295, n. 6, p. E1287–E1297, 2008. Citado na página 260.

JEONG, J. Y. et al. Transcriptional regulation of pyruvate dehydrogenase kinase. *Diabetes & metabolism journal*, Korean Diabetes Association, v. 36, n. 5, p. 328–335, 2012. Citado na página 272.

JEWARI, C. A.; BALDAUF, S. L. An excavate root for the eukaryote tree of life. *Science Advances*, American Association for the Advancement of Science, v. 9, n. 17, p. eade4973, 2023. Citado 2 vezes nas páginas 243 e 283.

JEZ, J. M.; CAHOON, R. E.; CHEN, S. Arabidopsis thaliana glutamate-cysteine ligase: functional properties, kinetic mechanism, and regulation of activity. *Journal of Biological Chemistry*, ASBMB, v. 279, n. 32, p. 33463–33470, 2004. Citado na página 197.

JONES, P. et al. Interproscan 5: genome-scale protein function classification. *Bioinformatics*, Oxford University Press, v. 30, n. 9, p. 1236–1240, 2014. Citado na página 105.

JU, L. et al. Diversity and distribution of freshwater testate amoebae (protozoa) along latitudinal and trophic gradients in china. *Microbial ecology*, Springer, v. 68, p. 657–670, 2014. Citado 2 vezes nas páginas 43 e 58.

JUHASZ, A. L. et al. Variability associated with as in vivo–in vitro correlations when using different bioaccessibility methodologies. *Environmental science & technology*, ACS Publications, v. 48, n. 19, p. 11646–11653, 2014. Citado na página 285.

KAIYALA, K. J.; RAMSAY, D. S. Direct animal calorimetry, the underused gold standard for quantifying the fire of life. *Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology*, Elsevier, v. 158, n. 3, p. 252–264, 2011. Citado na página 37.

KANG, S. et al. Between a pod and a hard test: the deep evolution of amoebae. *Molecular biology and evolution*, Oxford University Press, v. 34, n. 9, p. 2258–2270, 2017. Citado 6 vezes nas páginas 103, 104, 106, 136, 207 e 209.

KATOH, K. et al. Mafft: a novel method for rapid multiple sequence alignment based on fast fourier transform. *Nucleic acids research*, Oxford University Press, v. 30, n. 14, p. 3059–3066, 2002. Citado 3 vezes nas páginas 67, 68 e 328.

KATOH, K.; STANDLEY, D. M. Mafft multiple sequence alignment software version 7: improvements in performance and usability. *Molecular biology and evolution*, Society for Molecular Biology and Evolution, v. 30, n. 4, p. 772–780, 2013. Citado 2 vezes nas páginas 104 e 207.

KEELING, P. J.; PALMER, J. D. Horizontal gene transfer in eukaryotic evolution. *Nature Reviews Genetics*, Nature Publishing Group, v. 9, n. 8, p. 605–618, 2008. Citado na página 138.

KHAN, F. A.; ANSARI, A. A. Eutrophication: an ecological vision. *The botanical review*, Springer, v. 71, n. 4, p. 449–482, 2005. Citado 3 vezes nas páginas 52, 53 e 325.

KODALI, V. K.; THORPE, C. Oxidative protein folding and the quiescin–sulfhydryl oxidase family of flavoproteins. *Antioxidants & redox signaling*, Mary Ann Liebert, Inc. 140 Huguenot Street, 3rd Floor New Rochelle, NY 10801 USA, v. 13, n. 8, p. 1217–1230, 2010. Citado na página 199.

KOLISKO, M. et al. Single-cell transcriptomics for microbial eukaryotes. *Current Biology*, Elsevier, v. 24, n. 22, p. R1081–R1082, 2014. Citado na página 225.

KOSAKYAN, A. et al. Current and future perspectives on the systematics, taxonomy and nomenclature of testate amoebae. *European journal of protistology*, Elsevier, v. 55, p. 105–117, 2016. Citado 4 vezes nas páginas 40, 63, 82 e 275.

KOSAKYAN, A. et al. Coi barcoding of nebelid testate amoebae (amoebozoa: Arcellinida): extensive cryptic diversity and redefinition of the hyalospheniidae schultze. *Protist*, Elsevier, v. 163, n. 3, p. 415–434, 2012. Citado 2 vezes nas páginas 63 e 326.

KOSAKYAN, A.; LARA, E. Using testate amoebae communities to evaluate environmental stress: A molecular biology perspective. in: Nriagu, j.(ed.), encyclopedia of environmental health, volume 6. elsevier. Elsevier, 2019. Citado 2 vezes nas páginas 43 e 58.

KOSAKYAN, A. et al. Environmental dna coi barcoding for quantitative analysis of protists communities: A test using the nebela collaris complex (amoebozoa; arcellinida; hyalospheniidae). *European journal of protistology*, Elsevier, v. 51, n. 4, p. 311–320, 2015. Citado na página 328.

KREJSA, C. M. et al. Rapid activation of glutamate cysteine ligase following oxidative stress. *Journal of Biological Chemistry*, ASBMB, v. 285, n. 21, p. 16116–16124, 2010. Citado na página 197.

KUMAR, S. et al. Blobology: exploring raw genome data for contaminants, symbionts and parasites using taxon-annotated gc-coverage plots. *Frontiers in genetics*, Frontiers Media SA, v. 4, p. 237, 2013. Citado na página 208.

KUURI-RIUTTA, O.; VÄLIRANTA, M.; TUITTILA, E.-S. Literature review on testate amoebae as environmental indicators and as a functional part of the microbial community in northern peatlands. *Mires & Peat*, n. 28, 2022. Citado na página 286.

LADINO, G. et al. Ecosystem services provided by bromeliad plants: A systematic review. *Ecology and evolution*, Wiley Online Library, v. 9, n. 12, p. 7360–7372, 2019. Citado na página 39.

LAHR, D. J.; BERGMANN, P. J.; LOPES, S. G. Taxonomic identity in microbial eukaryotes: a practical approach using the testate amoeba centropyxis to resolve conflicts between old and new taxonomic descriptions. *Journal of Eukaryotic Microbiology*, Wiley Online Library, v. 55, n. 5, p. 409–416, 2008. Citado na página 69.

LAHR, D. J. et al. Comprehensive phylogenetic reconstruction of amoebozoa based on concatenated analyses of ssu-rdna and actin genes. *PLoS One*, Public Library of Science San Francisco, USA, v. 6, n. 7, p. e22780, 2011. Citado 2 vezes nas páginas 69 e 85.

LAHR, D. J. et al. How discordant morphological and molecular evolution among microorganisms can revise our notions of biodiversity on earth. *Bioessays*, Wiley Online Library, v. 36, n. 10, p. 950–959, 2014. Citado na página 63.

LAHR, D. J. et al. Phylogenomics and morphological reconstruction of arcellinida testate amoebae highlight diversity of microbial eukaryotes in the neoproterozoic. *Current Biology*, Elsevier, v. 29, n. 6, p. 991–1001, 2019. Citado 19 vezes nas páginas 7, 41, 42, 45, 63, 67, 69, 75, 78, 81, 85, 103, 104, 106, 136, 207, 209, 288 e 289.

LAMENTOWICZ, M. et al. Contrasting species—environment relationships in communities of testate amoebae, bryophytes and vascular plants along the fen–bog gradient. *Microbial Ecology*, Springer, v. 59, p. 499–510, 2010. Citado na página 345.

LANG, B. et al. The closest unicellular relatives of animals. *Current biology*, Elsevier, v. 12, n. 20, p. 1773–1778, 2002. Citado 2 vezes nas páginas 104 e 106.

LANSAC-TÔHA, F. et al. Structure of the testate amoebae community in different habitats in a neotropical floodplain. *Brazilian Journal of Biology*, SciELO Brasil, v. 74, n. 1, p. 181–190, 2014. Citado 2 vezes nas páginas 206 e 247.

LARA, E. et al. Ribosomal rna genes challenge the monophyly of the hyalospheniidae (amoebozoa: Arcellinida). *Protist*, Elsevier, v. 159, n. 2, p. 165–176, 2008. Citado 2 vezes nas páginas 64 e 81.

LAUMER, C. E. et al. Revisiting metazoan phylogeny with genomic sampling of all phyla. *Proceedings of the royal society B*, The Royal Society, v. 286, n. 1906, p. 20190831, 2019. Citado 2 vezes nas páginas 104 e 106.

LEGER, M. M. et al. Novel hydrogenosomes in the microaerophilic jakobid stygiella incarcerata. *Molecular biology and evolution*, Oxford University Press, v. 33, n. 9, p. 2318–2336, 2016. Citado 3 vezes nas páginas 205, 224 e 283.

LEGER, M. M. et al. Demystifying eukaryote lateral gene transfer (response to martin 2017 doi: 10.1002/bies. 201700115). *BioEssays*, Wiley Online Library, v. 40, n. 5, p. 1700242, 2018. Citado na página 138.

LEGER, M. M. et al. Evidence for a hydrogenosomal-type anaerobic atp generation pathway in acanthamoeba castellanii. *PLoS One*, Public Library of Science San Francisco, USA, v. 8, n. 9, p. e69532, 2013. Citado 2 vezes nas páginas 213 e 226.

LELIAERT, F. et al. Phylogeny and molecular evolution of the green algae. *Critical reviews in plant sciences*, Taylor & Francis, v. 31, n. 1, p. 1–46, 2012. Citado 2 vezes nas páginas 104 e 106.

LI, B.; DEWEY, C. N. Rsem: accurate transcript quantification from rna-seq data with or without a reference genome. *BMC bioinformatics*, Springer, v. 12, p. 1–16, 2011. Citado 2 vezes nas páginas 162 e 249.

LI, H.-S. et al. Hif-1θ protects against oxidative stress by directly targeting mitochondria. *Redox Biology*, Elsevier, v. 25, p. 101109, 2019. Citado na página 280.

LI, J. et al. Downregulation of smc1a inhibits growth and increases apoptosis and chemosensitivity of colorectal cancer cells. *Journal of International Medical Research*, SAGE Publications Sage UK: London, England, v. 44, n. 1, p. 67–74, 2016. Citado na página 200.

LIN, T.-C. et al. Phosphatidylinositol-5-phosphate 4-kinase gamma accumulates at the spindle pole and prevents microtubule depolymerization. *Cell Division*, Springer, v. 14, p. 1–14, 2019. Citado 2 vezes nas páginas 178 e 199.

LINDEQUE, P. K. et al. Next generation sequencing reveals the hidden diversity of zooplankton assemblages. *PloS one*, Public Library of Science San Francisco, USA, v. 8, n. 11, p. e81327, 2013. Citado na página 44.

LIU, W. et al. Knocking out acr2 does not affect arsenic redox status in arabidopsis thaliana: implications for as detoxification and accumulation in plants. *PloS one*, Public Library of Science, v. 7, n. 8, p. e42408, 2012. Citado 3 vezes nas páginas 134, 136 e 282.

LIU, Y.-C.; HUANG, H. Involvement of calcium-dependent protein kinase c in arsenite-induced genotoxicity in chinese hamster ovary cells. *Journal of cellular biochemistry*, Wiley Online Library, v. 64, n. 3, p. 423–433, 1997. Citado na página 195.

LIU, Z. et al. Single-cell transcriptomics of small microbial eukaryotes: limitations and potential. *The ISME Journal*, Nature Publishing Group, v. 11, n. 5, p. 1282–1285, 2017. Citado na página 44.

LÓPEZ-HERNÁNDEZ, T.; HAUCKE, V.; MARITZEN, T. Endocytosis in the adaptation to cellular stress. *Cell Stress*, Shared Science Publishers, v. 4, n. 10, p. 230, 2020. Citado na página 196.

LUSK, R. W. Diverse and widespread contamination evident in the unmapped depths of high throughput sequencing data. *PloS one*, Public Library of Science, v. 9, n. 10, p. e110808, 2014. Citado na página 105.

MACIASZCZYK-DZIUBINSKA, E.; WAWRZYCKA, D.; WYSOCKI, R. Arsenic and antimony transporters in eukaryotes. *International journal of molecular sciences*, Molecular Diversity Preservation International, v. 13, n. 3, p. 3527–3548, 2012. Citado na página 99.

MACINTYRE, N. R. Tissue hypoxia: implications for the respiratory clinician. *Respiratory care*, Respiratory Care, v. 59, n. 10, p. 1590–1596, 2014. Citado na página 246.

MACUMBER, A. L. et al. Phylogenetic divergence within the arcellinida (amoebozoa) is congruent with test size and metabolism type. *European Journal of Protistology*, Elsevier, v. 72, p. 125645, 2020. Citado na página 63.

MACUMBER, A. L. et al. Autoecological approaches to resolve subjective taxonomic divisions within arcellacea. *Protist*, Elsevier, v. 165, n. 3, p. 305–316, 2014. Citado 2 vezes nas páginas 206 e 247.

MADONI, P. Protozoa in wastewater treatment processes: a minireview. *Italian Journal of Zoology*, Taylor & Francis, v. 78, n. 1, p. 3–11, 2011. Citado na página 206.

MAHESWARI, S.; MURUGESAN, A. Remediation of arsenic in soil by aspergillus nidulans isolated from an arsenic-contaminated site. *Environmental technology*, Taylor & Francis, v. 30, n. 9, p. 921–926, 2009. Citado na página 138.

MALEK, M.; YAMPOLSKY, L. C. Severe hypoxia alters metabolism in daphnia by inducing gluconeogenesis. 2022. Citado na página 270.

MALYCH, R. et al. The response of naegleria gruberi to oxidative stress. *Metallomics*, Oxford Academic, v. 14, n. 3, 2022. Citado na página 268.

MANNI, M. et al. Busco update: novel and streamlined workflows along with broader and deeper phylogenetic coverage for scoring of eukaryotic, prokaryotic, and viral genomes. *Molecular biology and evolution*, Oxford University Press, v. 38, n. 10, p. 4647–4654, 2021. Citado 4 vezes nas páginas 162, 207, 209 e 249.

MARCHLER-BAUER, A. et al. Cdd: a conserved domain database for interactive domain family analysis. *Nucleic acids research*, Oxford University Press, v. 35, n. suppl_1, p. D237–D240, 2007. Citado na página 105.

MARCISZ, K. et al. Testate amoeba functional traits and their use in paleoecology. *Frontiers in Ecology and Evolution*, Frontiers Media SA, v. 8, p. 575966, 2020. Citado 4 vezes nas páginas 42, 62, 286 e 325.

MARSHALL, W. F. Regeneration in stentor coeruleus. *Frontiers in Cell and Developmental Biology*, Frontiers Media SA, v. 9, p. 753625, 2021. Citado na página 39.

MARTÍN-DURÁN, J. M. et al. A broad genomic survey reveals multiple origins and frequent losses in the evolution of respiratory hemerythrins and hemocyanins. *Genome biology and evolution*, Oxford University Press, v. 5, n. 7, p. 1435–1442, 2013. Citado na página 268.

MARTIN, M. Cutadapt removes adapter sequences from high-throughput sequencing reads. *EMBnet.journal*, v. 17, n. 1, p. 10–12, maio 2011. Disponível em: ⟨http://journal.embnet.org/index.php/embnetjournal/article/view/200⟩. Citado na página 328.

MARTIN, W. F. Too much eukaryote lgt. *BioEssays*, Wiley Online Library, v. 39, n. 12, p. 1700115, 2017. Citado na página 138.

MARTIN, W. F. Eukaryote lateral gene transfer is lamarckian. *Nature ecology & evolution*, Nature Publishing Group, v. 2, n. 5, p. 754–754, 2018. Citado na página 138.

MARTINS, M. d. Carmo de Carvalho e et al. Biological indicators of oxidative stress [malondialdehyde, catalase, glutathione peroxidase, and superoxide dismutase] and their application in nutrition. In: *Biomarkers in Nutrition*. [S.l.]: Springer, 2022. p. 1–25. Citado na página 197.

MAZEI, Y.; WARREN, A. A survey of the testate amoeba genus difflugia. 2017. Citado na página 40.

MCLEAN, C. et al. Harmful algal bloom-forming organism responds to nutrient stress distinctly from model phytoplankton. *bioRxiv*, Cold Spring Harbor Laboratory, p. 2021–02, 2021. Citado na página 198.

MEDIOLI, F.; SCOTT, D. B. Lacustrine thecamoebians (mainly arcellaceans) as potential tools for palaeolimnological interpretations. *Palaeogeography, Palaeoclimatology, Palaeoecology*, Elsevier, v. 62, n. 1-4, p. 361–386, 1988. Citado na página 275.

MEDIOLI, F.; SCOTT, D. B.; ABBOTT, B. A case study of protozoan intraclonal variability; taxonomic implications. *The Journal of Foraminiferal Research*, Cushman Foundation for Foraminiferal Research, v. 17, n. 1, p. 28–47, 1987. Citado 2 vezes nas páginas 63 e 326.

MEISTERFELD, R. Order arcellinida kent, 1880. *The illustrated guide to the Protozoa*, Society of Protozoologists Lawrence, Kansas, USA, v. 2, p. 827–860, 2002. Citado 5 vezes nas páginas 40, 42, 63, 275 e 325.

MELKONIAN, E. A.; SCHURY, M. P. Biochemistry, anaerobic glycolysis. 2019. Citado 2 vezes nas páginas 244 e 283.

MESSENS, J.; SILVER, S. Arsenate reduction: thiol cascade chemistry with convergent evolution. *Journal of molecular biology*, Elsevier, v. 362, n. 1, p. 1–17, 2006. Citado 3 vezes nas páginas 50, 100 e 159.

MEYER, J. [fefe] hydrogenases and their evolution: a genomic perspective. *Cellular and molecular life sciences*, Springer, v. 64, p. 1063–1084, 2007. Citado na página 283.

MINATEL, B. C. et al. Environmental arsenic exposure: From genetic susceptibility to pathogenesis. *Environment international*, Elsevier, v. 112, p. 183–197, 2018. Citado na página 158.

MINCHIN, P. An evaluation of relative robustness of techniques for ecological orderings. *Vegetatio*, v. 71, p. 145–156, 1987. Citado na página 329.

MITCHELL, E. A.; MEISTERFELD, R. Taxonomic confusion blurs the debate on cosmopolitanism versus local endemism of free-living protists. *Protist*, Elsevier, v. 156, n. 3, p. 263–267, 2005. Citado na página 285.

MIZRAHI, L.; ACHITUV, Y. Effect of heavy metals ions on enzyme activity in the mediterranean mussel, donax trunculus. *Bulletin of Environmental Contamination and Toxicology;(USA)*, v. 42, n. 6, 1989. Citado 2 vezes nas páginas 178 e 199.

MORALES, J. et al. Differential remodelling of peroxisome function underpins the environmental and metabolic adaptability of diplonemids and kinetoplastids. *Proceedings of the Royal Society B: Biological Sciences*, The Royal Society, v. 283, n. 1830, p. 20160520, 2016. Citado na página 271.

MORIN, G.; CALAS, G. Arsenic in soils, mine tailings, and former industrial sites. *Elements*, Mineralogical Association of Canada, v. 2, n. 2, p. 97–101, 2006. Citado 3 vezes nas páginas 46, 158 e 281.

MUENYI, C. S.; LJUNGMAN, M.; STATES, J. C. Arsenic disruption of dna damage responses—potential role in carcinogenesis and chemotherapy. *Biomolecules*, MDPI, v. 5, n. 4, p. 2184–2193, 2015. Citado na página 198.

MUKHOPADHYAY, R.; ZHOU, Y.; ROSEN, B. P. Directed evolution of a yeast arsenate reductase into a protein-tyrosine phosphatase. *Journal of Biological Chemistry*, ASBMB, v. 278, n. 27, p. 24476–24480, 2003. Citado na página 158.

MÜLLER, M. Energy metabolism: Part i: Anaerobic protozoa. In: *Molecular Medical Parasitology*. [S.l.]: Elsevier, 2003. p. 125–139. Citado 3 vezes nas páginas 227, 273 e 274.

MÜLLER, M. et al. Biochemistry and evolution of anaerobic energy metabolism in eukaryotes. *Microbiology and Molecular Biology Reviews*, Am Soc Microbiol, v. 76, n. 2, p. 444–495, 2012. Citado 7 vezes nas páginas 54, 206, 227, 243, 247, 271 e 273.

MULLER-PARKER, G.; D'ELIA, C. F.; COOK, C. B. Interactions between corals and their symbiotic algae. *Coral reefs in the Anthropocene*, Springer, p. 99–116, 2015. Citado na página 36.

MULOT, M. et al. Genetic determinism vs. phenotypic plasticity in protist morphology. *Journal of Eukaryotic Microbiology*, Wiley Online Library, v. 64, n. 6, p. 729–739, 2017. Citado 2 vezes nas páginas 41 e 63.

MUÑOZ-GÓMEZ, S. A. Energetics and evolution of anaerobic microbial eukaryotes. *Nature Microbiology*, Nature Publishing Group UK London, p. 1–7, 2023. Citado na página 243.

MURRAY, L. A. et al. Biotransformation of arsenate to arsenosugars by chlorella vulgaris. *Applied organometallic chemistry*, Wiley Online Library, v. 17, n. 9, p. 669–674, 2003. Citado na página 137.

NAIYER, S.; BHATTACHARYA, A.; BHATTACHARYA, S. Advances in entamoeba histolytica biology through transcriptomic analysis. *Frontiers in microbiology*, Frontiers Media SA, v. 10, p. 1921, 2019. Citado na página 280.

NASSER, N. et al. Utility of arcellaceans (shelled protists) as a tool for monitoring arsenic and heavy metal contamination. In: *Latornell Conservation Symposium, Geosciences*. [S.l.: s.n.], 2014. Citado 4 vezes nas páginas 46, 160, 194 e 285.

NASSER, N. A. et al. Lacustrine arcellinina (testate amoebae) as bioindicators of arsenic contamination. *Microbial ecology*, Springer, v. 72, n. 1, p. 130–149, 2016. Citado 10 vezes nas páginas 9, 51, 52, 101, 136, 160, 194, 206, 247 e 284.

NASSER, N. A. et al. Use of arcellinida (testate lobose amoebae) arsenic tolerance limits as a novel tool for biomonitoring arsenic contamination in lakes. *Ecological Indicators*, Elsevier, v. 113, p. 106177, 2020. Citado 8 vezes nas páginas 43, 62, 101, 136, 160, 194, 285 e 325.

NÉMETI, B.; ANDERSON, M. E.; GREGUS, Z. Glutathione synthetase promotes the reduction of arsenate via arsenolysis of glutathione. *Biochimie*, Elsevier, v. 94, n. 6, p. 1327–1333, 2012. Citado na página 282.

NEYT, C. et al. Virulence and arsenic resistance in yersiniae. *Journal of Bacteriology*, Am Soc Microbiol, v. 179, n. 3, p. 612–619, 1997. Citado na página 159.

NGUYEN, J.; LARA-GUTIÉRREZ, J.; STOCKER, R. Environmental fluctuations and their effects on microbial communities, populations and individuals. *FEMS microbiology reviews*, Oxford University Press, v. 45, n. 4, p. fuaa068, 2021. Citado 2 vezes nas páginas 280 e 286.

NGUYEN, L.-T. et al. Iq-tree: a fast and effective stochastic algorithm for estimating maximum-likelihood phylogenies. *Molecular biology and evolution*, Oxford University Press, v. 32, n. 1, p. 268–274, 2015. Citado 5 vezes nas páginas 67, 68, 105, 209 e 328.

NIKOLAIDIS, N. P. et al. Arsenic mobility in contaminated lake sediments. *Environmental Pollution*, Elsevier, v. 129, n. 3, p. 479–487, 2004. Citado na página 46.

NISHINO, K. et al. Function and inhibitory mechanisms of multidrug efflux pumps. *Frontiers in Microbiology*, Frontiers Media SA, v. 12, p. 737288, 2021. Citado na página 196.

NOVOSEL, N. et al. Salinity-induced chemical, mechanical, and behavioral changes in marine microalgae. *Journal of applied phycology*, Springer, v. 34, n. 3, p. 1293–1309, 2022. Citado na página 280.

NOZAKI, K. et al. A new na+/h+ antiporter, nhad, of vibrio parahaemolyticus. *Biochimica et Biophysica Acta (BBA)-Biomembranes*, Elsevier, v. 1369, n. 2, p. 213–220, 1998. Citado 2 vezes nas páginas 108 e 109.

NÝVLTOVÁ, E. et al. Lateral gene transfer and gene duplication played a key role in the evolution of mastigamoeba balamuthi hydrogenosomes. *Molecular biology and evolution*, Oxford University Press, v. 32, n. 4, p. 1039–1055, 2015. Citado 8 vezes nas páginas 205, 207, 216, 217, 224, 226, 227 e 273.

OHLMEIER, S. et al. The yeast mitochondrial proteome, a study of fermentative and respiratory growth. *Journal of Biological Chemistry*, ASBMB, v. 279, n. 6, p. 3956–3979, 2004. Citado na página 196.

OPPERDOES, F. R.; JONCKHEERE, J. F. D.; TIELENS, A. G. Naegleria gruberi metabolism. *International journal for parasitology*, Elsevier, v. 41, n. 9, p. 915–924, 2011. Citado 2 vezes nas páginas 227 e 273.

OREMLAND, R. S. et al. Arsenic in the evolution of earth and extraterrestrial ecosystems. *Geomicrobiology Journal*, Taylor & Francis, v. 26, n. 7, p. 522–536, 2009. Citado na página 100.

OREMLAND, R. S.; STOLZ, J. F. The ecology of arsenic. *Science*, American Association for the Advancement of Science, v. 300, n. 5621, p. 939–944, 2003. Citado 2 vezes nas páginas 133 e 140.

ORGANIZATION, W. H. et al. Global malaria control and elimination: report of a technical review. World Health Organization, 2008. Citado na página 36.

ORGANIZATION, W. H. et al. Who global strategy on health, environment and climate change: the transformation needed to improve lives and wellbeing sustainably through healthy environments. World Health Organization, 2020. Citado na página 39.

ORTIZ, A. T. et al. The testate lobose amoebae in the wastewater treatment. In: *Current Research Topics In Applied Microbiology And Microbial Biotechnology*. [S.l.]: World Scientific, 2009. p. 347–351. Citado 2 vezes nas páginas 43 e 58.

OSADA, M. et al. Nadph-cytochrome p-450 reductase in the plasma membrane modulates the activation of hypoxia-inducible factor 1. *Journal of Biological Chemistry*, ASBMB, v. 277, n. 26, p. 23367–23373, 2002. Citado 2 vezes nas páginas 263 e 268.

PALMER, M. J. et al. Seasonal variation of arsenic and antimony in surface waters of small subarctic lakes impacted by legacy mining pollution near yellowknife, nt, canada. *Science of the Total Environment*, Elsevier, v. 684, p. 326–339, 2019. Citado na página 46.

PALMGREN, M. et al. As3mt-mediated tolerance to arsenic evolved by multiple independent horizontal gene transfers from bacteria to eukaryotes. *PloS one*, Public Library of Science, v. 12, n. 4, 2017. Citado 4 vezes nas páginas 102, 120, 132 e 133.

PARFREY, L. W. et al. Estimating the timing of early eukaryotic diversification with multigene molecular clocks. *Proceedings of the National Academy of Sciences*, National Acad Sciences, v. 108, n. 33, p. 13624–13629, 2011. Citado 3 vezes nas páginas 104, 106 e 205.

PARK, C.-J.; SEO, Y.-S. Heat shock proteins: a review of the molecular chaperones for plant immunity. *The plant pathology journal*, The Korean Society of Plant Pathology, v. 31, n. 4, p. 323, 2015. Citado na página 199.

PARK, J.-H. et al. Role of phospholipase d in the lifespan of caenorhabditis elegans. *Experimental & Molecular Medicine*, Nature Publishing Group UK London, v. 50, n. 4, p. 1–10, 2018. Citado 2 vezes nas páginas 182 e 195.

PATTERSON, R.; BAKER, T.; BURBIDGE, S. Arcellaceans (thecamoebians) as proxies of arsenic and mercury contamination in northeastern ontario lakes. *The Journal of Foraminiferal Research*, Cushman Foundation for Foraminiferal Research, v. 26, n. 2, p. 172–183, 1996. Citado 2 vezes nas páginas 194 e 285.

PATTERSON, R. T. et al. Arcellinida (testate lobose amoebae) as sensitive bioindicators of arsenic contamination in lakes. In: *Exploring the Nexus of Geoecology, Geography, Geoarcheology and Geotourism: Advances and Applications for Sustainable Development in Environmental Sciences and Agroforestry Research*. [S.l.]: Springer, 2019. p. 71–73. Citado 11 vezes nas páginas 9, 43, 48, 51, 52, 58, 101, 136, 160, 194 e 285.

PAWLOWSKI, J.; HOLZMANN, M.; TYSZKA, J. New supraordinal classification of foraminifera: Molecules meet morphology. *Marine Micropaleontology*, Elsevier, v. 100, p. 1–10, 2013. Citado na página 63.

PAYNE, R. J.; LAMENTOWICZ, M.; MITCHELL, E. A. The perils of taxonomic inconsistency in quantitative palaeoecology: experiments with testate amoeba data. *Boreas*, Wiley Online Library, v. 40, n. 1, p. 15–27, 2011. Citado na página 285.

PEDERSEN, J. T. et al. Predicted as3mt proteins methylate arsenic and support two major phylogenetic as3mt groups. *Chemical research in toxicology*, ACS Publications, v. 33, n. 12, p. 3041–3047, 2020. Citado 2 vezes nas páginas 121 e 122.

PFEIFFER, T.; SCHUSTER, S.; BONHOEFFER, S. Cooperation and competition in the evolution of atp-producing pathways. *Science*, American Association for the Advancement of Science, v. 292, n. 5516, p. 504–507, 2001. Citado 2 vezes nas páginas 226 e 276.

PICELLI, S. et al. Full-length rna-seq from single cells using smart-seq2. *Nature protocols*, Nature Publishing Group, v. 9, n. 1, p. 171, 2014. Citado 3 vezes nas páginas 59, 161 e 249.

PIÑA-OCHOA, E. et al. Widespread occurrence of nitrate storage and denitrification among foraminifera and gromiida. *Proceedings of the National Academy of Sciences*, National Acad Sciences, v. 107, n. 3, p. 1148–1153, 2010. Citado na página 246.

PINEDA, E. et al. Pyruvate: ferredoxin oxidoreductase and bifunctional aldehyde–alcohol dehydrogenase are essential for energy metabolism under oxidative stress in entamoeba histolytica. *The FEBS journal*, Wiley Online Library, v. 277, n. 16, p. 3382–3395, 2010. Citado 2 vezes nas páginas 226 e 276.

PINTO, G. et al. Species composition of cyanidiales assemblages in pisciarelli (campi flegrei, italy) and description of galdieria phlegrea sp. nov. In: *Algae and cyanobacteria in extreme environments*. [S.l.]: Springer, 2007. p. 487–502. Citado 3 vezes nas páginas 101, 137 e 282.

PIRKL, F.; BUCHNER, J. Functional analysis of the hsp90-associated human peptidyl prolyl cis/trans isomerases fkbp51, fkbp52 and cyp40. *Journal of molecular biology*, Elsevier, v. 308, n. 4, p. 795–806, 2001. Citado na página 199.

PISANI, D.; COTTON, J. A.; MCINERNEY, J. O. Supertrees disentangle the chimerical origin of eukaryotic genomes. *Molecular Biology and Evolution*, Oxford University Press, v. 24, n. 8, p. 1752–1760, 2007. Citado na página 223.

PORFÍRIO-SOUSA, A. L.; RIBEIRO, G. M.; LAHR, D. J. Morphometric and genetic analysis of arcella intermedia and arcella intermedia laevis (amoebozoa, arcellinida) illuminate phenotypic plasticity in microbial eukaryotes. *European journal of protistology*, Elsevier, v. 58, p. 187–194, 2017. Citado 9 vezes nas páginas 41, 45, 59, 63, 65, 67, 69, 289 e 326.

PORTER, S. M. Insights into eukaryogenesis from the fossil record. *Interface Focus*, The Royal Society, v. 10, n. 4, p. 20190105, 2020. Citado na página 140.

PRAKASH, S. et al. The ion transporter superfamily. *Biochimica et Biophysica Acta (BBA)-Biomembranes*, Elsevier, v. 1618, n. 1, p. 79–92, 2003. Citado 2 vezes nas páginas 108 e 109.

PROCHOWNIK, E. V.; WANG, H. The metabolic fates of pyruvate in normal and neoplastic cells. *Cells*, MDPI, v. 10, n. 4, p. 762, 2021. Citado 2 vezes nas páginas 206 e 247.

PUCER, A. et al. Differential role of cathepsins b and l in autophagy-associated cell death induced by arsenic trioxide in u87 human glioblastoma cells. *Biological chemistry*, De Gruyter, v. 391, n. 5, p. 519–531, 2010. Citado na página 200.

QIN, J. et al. Arsenic detoxification and evolution of trimethylarsine gas by a microbial arsenite s-adenosylmethionine methyltransferase. *Proceedings of the National Academy of Sciences*, National Acad Sciences, v. 103, n. 7, p. 2075–2080, 2006. Citado 5 vezes nas páginas 50, 99, 122, 132 e 159.

QIU, H. et al. Adaptation through horizontal gene transfer in the cryptoendolithic red alga galdieria phlegrea. *Current Biology*, Elsevier, v. 23, n. 19, p. R865–R866, 2013. Citado 3 vezes nas páginas 205, 225 e 283.

RAHAMAN, M. S.; MISE, N.; ICHIHARA, S. Arsenic contamination in food chain in bangladesh: A review on health hazards, socioeconomic impacts and implications. *Hygiene and Environmental Health Advances*, Elsevier, v. 2, p. 100004, 2022. Citado na página 160.

RAN, S.; LIU, J.; LI, S. A systematic review of the various effect of arsenic on glutathione synthesis in vitro and in vivo. *BioMed Research International*, Hindawi, v. 2020, 2020. Citado na página 282.

RAY, P. D.; HUANG, B.-W.; TSUJI, Y. Reactive oxygen species (ros) homeostasis and redox regulation in cellular signaling. *Cellular signalling*, Elsevier, v. 24, n. 5, p. 981–990, 2012. Citado na página 269.

REGALADO, I. S. et al. Ecological drivers of testate amoeba diversity in tropical water bodies of central mexico. *Journal of Limnology*, PAGEPress Publications, v. 77, n. 3, 2018. Citado 2 vezes nas páginas 43 e 58.

REICHARD, J. F.; PUGA, A. Effects of arsenic exposure on dna methylation and epigenetic gene regulation. *Epigenomics*, Future Medicine, v. 2, n. 1, p. 87–104, 2010. Citado na página 158.

REINHARD, C. T. et al. Earth's oxygen cycle and the evolution of animal life. *Proceedings of the National Academy of Sciences*, National Academy of Sciences, v. 113, n. 32, p. 8933–8938, 2016. ISSN 0027-8424. Disponível em: ⟨http://www.pnas.org/content/113/32/8933⟩. Citado na página 243.

REIS, V.; DUARTE, A. C. Occurrence, distribution, and significance of arsenic speciation. In: *Comprehensive Analytical Chemistry*. [S.l.]: Elsevier, 2019. v. 85, p. 1–14. Citado na página 158.

RIBEIRO, G. M.; LAHR, D. J. A comparative study indicates vertical inheritance and horizontal gene transfer of arsenic resistance-related genes in eukaryotes. *Molecular Phylogenetics and Evolution*, Elsevier, v. 173, p. 107479, 2022. Citado 10 vezes nas páginas 44, 45, 160, 175, 190, 194, 196, 282, 283 e 289.

RIBEIRO, G. M. et al. De novo sequencing, assembly, and annotation of the transcriptome for the free-living testate amoeba arcella intermedia. *journal of eukaryotic microbiology*, Wiley Online Library, v. 67, n. 3, p. 383–392, 2020. Citado 6 vezes nas páginas 45, 46, 59, 67, 160 e 289.

RIBEIRO, G. M. et al. Growth rate modulation enables coexistence in a competitive exclusion scenario between microbial eukaryotes. *Acta Protozoologica*, v. 58, n. 4, p. 217–233, 2019. Citado 9 vezes nas páginas 45, 59, 65, 67, 161, 248, 250, 286 e 289.

RICHARDS, T. A. et al. Gene transfer into the fungi. *Fungal Biology Reviews*, Elsevier, v. 25, n. 2, p. 98–110, 2011. Citado na página 138.

RICHTER, D. J. et al. Eukprot: a database of genome-scale predicted proteins across the diversity of eukaryotic life. *BioRxiv*, Cold Spring Harbor Laboratory, 2020. Citado na página 103.

RIGOULET, M. et al. Cell energy metabolism: An update. *Biochimica et Biophysica Acta (BBA)-Bioenergetics*, Elsevier, v. 1861, n. 11, p. 148276, 2020. Citado na página 54.

ROBBINS, D. et al. Isocitrate dehydrogenase 1 is downregulated during early skin tumorigenesis which can be inhibited by overexpression of manganese superoxide dismutase. *Cancer science*, Wiley Online Library, v. 103, n. 8, p. 1429–1433, 2012. Citado 3 vezes nas páginas 260, 272 e 273.

ROBINSON, M. D.; MCCARTHY, D. J.; SMYTH, G. K. edger: a bioconductor package for differential expression analysis of digital gene expression data. *bioinformatics*, Oxford University Press, v. 26, n. 1, p. 139–140, 2010. Citado 2 vezes nas páginas 162 e 250.

RODRÍGUEZ-MARTÍN, D. et al. Arsenate and arsenite differential toxicity in tetrahymena thermophila. *Journal of Hazardous Materials*, Elsevier, v. 431, p. 128532, 2022. Citado 2 vezes nas páginas 160 e 282.

RODRIGUEZ, M. A. et al. The pyruvate: ferredoxin oxidoreductase enzyme is located in the plasma membrane and in a cytoplasmic structure inentamoeba. *Microbial pathogenesis*, Elsevier, v. 25, n. 1, p. 1–10, 1998. Citado na página 247.

ROE, H. M.; PATTERSON, R. T. Arcellacea (testate amoebae) as bio-indicators of road salt contamination in lakes. *Microbial ecology*, Springer, v. 68, n. 2, p. 299–313, 2014. Citado 6 vezes nas páginas 43, 58, 194, 206, 247 e 285.

ROE, H. M.; PATTERSON, R. T.; SWINDLES, G. T. Controls on the contemporary distribution of lake thecamoebians (testate amoebae) within the greater toronto area and their potential as water quality indicators. *Journal of Paleolimnology*, Springer, v. 43, n. 4, p. 955–975, 2010. Citado 10 vezes nas páginas 43, 46, 58, 83, 206, 247, 248, 266, 284 e 325.

ROGNES, T. et al. Vsearch: a versatile open source tool for metagenomics. *PeerJ*, PeerJ Inc., v. 4, p. e2584, 2016. Citado na página 328.

ROSEN, B. The plasmid-encoded arsenical resistance pump: an anion-translocating atpase. *Research in microbiology*, Elsevier, v. 141, n. 3, p. 336–341, 1990. Citado 4 vezes nas páginas 49, 50, 99 e 159.

ROSWELL, M.; DUSHOFF, J.; WINFREE, R. A conceptual guide to measuring species diversity. *Oikos*, Wiley Online Library, v. 130, n. 3, p. 321–338, 2021. Citado na página 329.

ROTTE, C. et al. Pyruvate: Nadp oxidoreductase from the mitochondrion of euglena gracilis and from the apicomplexan cryptosporidium parvum: a biochemical relic linking pyruvate metabolism in mitochondriate and amitochondriate protists. *Molecular Biology and Evolution*, Oxford University Press, v. 18, n. 5, p. 710–720, 2001. Citado 2 vezes nas páginas 206 e 247.

ROTTEROVÁ, J. et al. Genomics of new ciliate lineages provides insight into the evolution of obligate anaerobiosis. *Current Biology*, Elsevier, v. 30, n. 11, p. 2037–2050, 2020. Citado na página 243.

RUGGIERO, A. et al. High diversity of testate amoebae (amoebozoa, arcellinida) detected by hts analyses in a new england fen using newly designed taxon-specific primers. *Journal of Eukaryotic Microbiology*, Wiley Online Library, v. 67, n. 4, p. 450–462, 2020. Citado na página 81.

RUKH, S. et al. An overview of arsenic extraction and speciation techniques in soil and water. *Amer. Chem. Sci. J*, v. 6, p. 1–15, 2015. Citado na página 48.

RUSSELL, B. et al. The directiveness of organic activities. *The directiveness of organic activities.*, CambridgeUniversity Press, 1944. Citado na página 275.

SABIR, S. et al. Role of cadmium and arsenic as endocrine disruptors in the metabolism of carbohydrates: inserting the association into perspectives. *Biomedicine & pharmacotherapy*, Elsevier, v. 114, p. 108802, 2019. Citado na página 198.

SACHS, J. et al. *Sustainable development report 2022*. [S.l.]: Cambridge University Press, 2022. Citado na página 40.

SAGA, Y.; OKADA, H.; YANAGISAWA, K. Macrocyst development in dictyostelium discoideum. ii. mating-type-specific cell fusion and acquisition of fusion-competence. *Journal of Cell Science*, Company of Biologists The Company of Biologists, Bidder Building, 140 Cowley . . . , v. 60, n. 1, p. 157–168, 1983. Citado 2 vezes nas páginas 200 e 286.

SAHU, Y. K.; JAIN, M. Study of seasonal physiochemical parameters and quality assessment of lake water in raipur city, chhattisgarh. Citado na página 344.

SANCHEZ, L. B.; MÜLLER, M. Purification and characterization of the acetate forming enzyme, acetyl-coa synthetase (adp-forming) from the amitochondriate protist, giardia lamblia. *FEBS letters*, Wiley Online Library, v. 378, n. 3, p. 240–244, 1996. Citado 4 vezes nas páginas 205, 227, 273 e 283.

SARKAR, S. et al. Low dose of arsenic trioxide triggers oxidative stress in zebrafish brain: expression of antioxidant genes. *Ecotoxicology and environmental safety*, Elsevier, v. 107, p. 1–8, 2014. Citado na página 197.

SCHAAP, P.; SCHILDE, C. Encystation: the most prevalent and underinvestigated differentiation pathway of eukaryotes. *Microbiology*, Microbiology Society, v. 164, n. 5, p. 727–739, 2018. Citado na página 280.

SCHNEIDER, C. A.; RASBAND, W. S.; ELICEIRI, K. W. Nih image to imagej: 25 years of image analysis. *Nature methods*, Nature Publishing Group, v. 9, n. 7, p. 671–675, 2012. Citado 2 vezes nas páginas 65 e 66.

SCHÖNENBERGER, M. J.; KOVACS, W. J. Hypoxia signaling pathways: modulators of oxygen-related organelles. *Frontiers in cell and developmental biology*, Frontiers Media SA, v. 3, p. 42, 2015. Citado na página 280.

SCHÖNKNECHT, G. et al. Gene transfer from bacteria and archaea facilitated evolution of an extremophilic eukaryote. *Science*, American Association for the Advancement of Science, v. 339, n. 6124, p. 1207–1210, 2013. Citado 4 vezes nas páginas 102, 124, 132 e 133.

SCHULZ, G. et al. Evaluation of morphological characteristics to delineate taxa of the genus trigonopyxis (amoebozoa, arcellinida). *Protist*, Elsevier, v. 169, n. 2, p. 190–205, 2018. Citado na página 63.

SCHWEDERSKY, R. P. et al. The anaphase promoting complex/cyclosome subunit 11 and its role in organ size and plant development. *Frontiers in Plant Science*, Frontiers Media SA, v. 12, p. 563760, 2021. Citado na página 200.

SEAL, S. V.; TURNER, J. D. The 'jekyll and hyde'of gluconeogenesis: early life adversity, later life stress, and metabolic disturbances. *International Journal of Molecular Sciences*, MDPI, v. 22, n. 7, p. 3344, 2021. Citado na página 198.

SENN, D. B.; HEMOND, H. F. Particulate arsenic and iron during anoxia in a eutrophic, urban lake. *Environmental Toxicology and Chemistry: An International Journal*, Wiley Online Library, v. 23, n. 7, p. 1610–1616, 2004. Citado na página 46.

SEYFFERTH, C. et al. Advances and opportunities in single-cell transcriptomics for plant research. *Annual review of plant biology*, Annual Reviews, v. 72, p. 847–866, 2021. Citado na página 44.

SHEN, J. et al. The saccharomyces cerevisiae arr4p is involved in metal and heat tolerance. *Biometals*, Springer, v. 16, n. 3, p. 369–378, 2003. Citado na página 111.

SHEN, Z.-Y. et al. Nitric oxide and calcium ions in apoptotic esophageal carcinoma cells induced by arsenite. *World Journal of Gastroenterology*, Baishideng Publishing Group Inc, v. 8, n. 1, p. 40, 2002. Citado na página 195.

SHETTY, P.; GITAU, M. M.; MARÓTI, G. Salinity stress responses and adaptation mechanisms in eukaryotic green microalgae. *Cells*, MDPI, v. 8, n. 12, p. 1657, 2019. Citado na página 280.

SHIMODAIRA, H. An approximately unbiased test of phylogenetic tree selection. *Systematic biology*, Oxford University Press, v. 51, n. 3, p. 492–508, 2002. Citado na página 106.

SIERACKI, M. E. et al. Single cell genomics yields a wide diversity of small planktonic protists across major ocean ecosystems. *Scientific reports*, Nature Publishing Group UK London, v. 9, n. 1, p. 6025, 2019. Citado na página 44.

SIKDAR, S. *Fundamentals and Applications of Bioremediation: Principles*. [S.l.]: Routledge, 2017. v. 1. Citado na página 205.

SILVA, C. d. L. et al. Evaluation of sediment contamination by trace elements and the zooplankton community analysis in area affected by gold exploration in southeast (se) of the iron quadrangle, alto rio doce,(mg) brazil. *Acta Limnologica Brasiliensia*, SciELO Brasil, v. 25, n. 2, p. 150–157, 2013. Citado 5 vezes nas páginas 43, 58, 206, 247 e 248.

SILVER, S.; PHUNG, L. T. Genes and enzymes involved in bacterial oxidation and reduction of inorganic arsenic. *Appl. Environ. Microbiol.*, Am Soc Microbiol, v. 71, n. 2, p. 599–608, 2005. Citado 3 vezes nas páginas 49, 100 e 159.

SIMION, P.; DELSUC, F.; PHILIPPE, H. *To What Extent Current Limits of Phylogenomics Can Be Overcome?* [S.l.]: No commercial publisher— Authors open access book, 2020. Citado na página 105.

SINGER, D. et al. Environmental filtering and phylogenetic clustering correlate with the distribution patterns of cryptic protist species. *Ecology*, Wiley Online Library, v. 99, n. 4, p. 904–914, 2018. Citado na página 81.

SINGH, R. et al. Improved annotation with de novo transcriptome assembly in four social amoeba species. *BMC genomics*, BioMed Central, v. 18, n. 1, p. 120, 2017. Citado na página 225.

ŠKODOVÁ-SVERÁKOVÁ, I. et al. Highly flexible metabolism of the marine euglenozoan protist diplonema papillatum. *BMC biology*, BioMed Central, v. 19, n. 1, p. 1–21, 2021. Citado 3 vezes nas páginas 198, 271 e 273.

SMITH, H. G.; BOBROV, A.; LARA, E. Diversity and biogeography of testate amoebae. *Protist Diversity and Geographical Distribution*, Springer, p. 95–109, 2009. Citado 2 vezes nas páginas 42 e 344.

SNAITH, H. A.; MARLETT, J.; FORSBURG, S. L. Ibp1p, a novel cdc25-related phosphatase, suppresses schizosaccharomyces pombe hsk1 (cdc7). *Current genetics*, Springer, v. 44, n. 1, p. 38–48, 2003. Citado na página 134.

SOLER-ZAMORA, C. et al. Arcellinida testate amoebae as climate miner's canaries in southern spain. *European Journal of Protistology*, Elsevier, v. 81, p. 125828, 2021. Citado 3 vezes nas páginas 62, 80 e 325.

SOUTO, M. S. et al. Distribution of testate amoebae in bryophyte communities in são miguel island (azores archipelago). *Biodiversity data journal*, Pensoft Publishers, v. 9, 2021. Citado na página 83.

STAIRS, C. W. et al. A suf fe-s cluster biogenesis system in the mitochondrion-related organelles of the anaerobic protist pygsuia. *Current Biology*, Elsevier, v. 24, n. 11, p. 1176–1186, 2014. Citado na página 205.

STAIRS, C. W.; LEGER, M. M.; ROGER, A. J. Diversity and origins of anaerobic metabolism in mitochondria and related organelles. *Phil. Trans. R. Soc. B*, The Royal Society, v. 370, n. 1678, p. 20140326, 2015. Citado 8 vezes nas páginas 29, 54, 58, 207, 208, 243, 271 e 283.

STAIRS, C. W. et al. Anaeramoebae are a divergent lineage of eukaryotes that shed light on the transition from anaerobic mitochondria to hydrogenosomes. *Current Biology*, Elsevier, 2021. Citado na página 138.

STAMATI, K.; MUDERA, V.; CHEEMA, U. Evolution of oxygen utilization in multicellular organisms and implications for cell signalling in tissue engineering. *Journal of tissue engineering*, SAGE Publications Sage UK: London, England, v. 2, n. 1, p. 2041731411432365, 2011. Citado na página 243.

STEFFEN, W. et al. The anthropocene: are humans now overwhelming the great forces of nature. *Ambio-Journal of Human Environment Research and Management*, [Stockholm]: Royal Swedish Academy of Sciences;[Boston: Universitetsforlaget . . . , v. 36, n. 8, p. 614–621, 2007. Citado na página 40.

STEINBÜCHEL, A.; MÜLLER, M. Anaerobic pyruvate metabolism of tritrichomonas foetus and trichomonas vaginalis hydrogenosomes. *Molecular and biochemical parasitology*, Elsevier, v. 20, n. 1, p. 57–65, 1986. Citado na página 271.

SULASTRI, S. H. N.; AKHDIANA, I. Temporal variation of physico-chemical characteristics and phytoplankton composition of three urban lakes in cibinong, west java, indonesia. *AACL Bioflux*, v. 14, n. 3, 2021. Citado na página 344.

SUNG, H.-J. et al. Quiescin sulfhydryl oxidase 1 (qsox1) secreted by lung cancer cells promotes cancer metastasis. *International Journal of Molecular Sciences*, MDPI, v. 19, n. 10, p. 3213, 2018. Citado na página 199.

SWAIN, R.; ROUT, G. R. Silicon mediated alleviation of salinity stress regulated by silicon transporter genes (lsi1 and lsi2) in indica rice. *Brazilian Archives of Biology and Technology*, SciELO Brasil, v. 63, 2020. Citado 2 vezes nas páginas 108 e 109.

TAM, L. M.; PRICE, N. E.; WANG, Y. Molecular mechanisms of arsenic-induced disruption of dna repair. *Chemical research in toxicology*, ACS Publications, v. 33, n. 3, p. 709–726, 2020. Citado na página 198.

TAMAKI, S.; JR, W. F. Environmental biochemistry of arsenic. *Reviews of Environmental Contamination and Toxicology: Continuation of Residue Reviews*, Springer, p. 79–110, 1992. Citado na página 195.

TAMRAKAR, A.; UPADHYAY, K.; BAJPAI, S. Spatial variation of physico-chemical parameters and water quality assessment of urban ponds at raipur, chhattisgarh, india. In: IOP PUBLISHING. *IOP Conference Series: Earth and Environmental Science*. [S.l.], 2022. v. 1032, n. 1, p. 012034. Citado na página 344.

TANAKA, T. Distribution of arsenic in the natural environment with emphasis on rocks and soils. *Applied Organometallic Chemistry*, Wiley Online Library, v. 2, n. 4, p. 283–295, 1988. Citado na página 99.

TANG, Y. et al. Impact of eutrophication on arsenic cycling in freshwaters. *Water research*, Elsevier, v. 150, p. 191–199, 2019. Citado na página 137.

TAWFIK, D. S.; VIOLA, R. E. Arsenate replacing phosphate: alternative life chemistries and ion promiscuity. *Biochemistry*, ACS Publications, v. 50, n. 7, p. 1128–1134, 2011. Citado na página 198.

TEAM, R. R. C. et al. R: A language and environment for statistical computing. Vienna, Austria, 2013. Citado na página 328.

TEDERSOO, L. et al. High-level classification of the fungi and a tool for evolutionary ecological analyses. *Fungal Diversity*, Springer, v. 90, n. 1, p. 135–159, 2018. Citado 2 vezes nas páginas 104 e 106.

THAKUR, R.; SHIRATORI, T.; ISHIDA, K.-i. Taxon-rich multigene phylogenetic analyses resolve the phylogenetic relationship among deep-branching stramenopiles. *Protist*, Elsevier, v. 170, n. 5, p. 125682, 2019. Citado 2 vezes nas páginas 104 e 106.

THOMAS, D. J. et al. Arsenic (+ 3 oxidation state) methyltransferase and the methylation of arsenicals. *Experimental Biology and Medicine*, SAGE Publications, v. 232, n. 1, p. 3–13, 2007. Citado 3 vezes nas páginas 50, 99 e 159.

THORPE, C.; COPPOCK, D. L. Generating disulfides in multicellular organisms: emerging roles for a new flavoprotein family. *Journal of Biological Chemistry*, ASBMB, v. 282, n. 19, p. 13929–13933, 2007. Citado 2 vezes nas páginas 178 e 199.

TICE, A. K. et al. Expansion of the molecular and morphological diversity of acanthamoebidae (centramoebida, amoebozoa) and identification of a novel life cycle type within the group. *Biology direct*, BioMed Central, v. 11, n. 1, p. 69, 2016. Citado 2 vezes nas páginas 207 e 209.

TIELENS, A. G. et al. Acetate formation in the energy metabolism of parasitic helminths and protists. *International journal for parasitology*, Elsevier, v. 40, n. 4, p. 387–397, 2010. Citado na página 226.

TIELENS, A. G. et al. Mitochondria as we don't know them. *Trends in biochemical sciences*, Elsevier, v. 27, n. 11, p. 564–572, 2002. Citado na página 247.

TSAOUSIS, A. D. et al. The biochemical adaptations of mitochondrion-related organelles of parasitic and free-living microbial eukaryotes to low oxygen environments. In: *Anoxia*. [S.l.]: Springer, 2012. p. 51–81. Citado 2 vezes nas páginas 205 e 276.

TSENG, Y.-Y.; YU, C.-W.; LIAO, V. H.-C. Caenorhabditis elegans expresses a functional arsa. *The FEBS journal*, Wiley Online Library, v. 274, n. 10, p. 2566–2572, 2007. Citado na página 111.

TYLER, R. M.; BRADY, D. C.; TARGETT, T. E. Temporal and spatial dynamics of diel-cycling hypoxia in estuarine tributaries. *Estuaries and Coasts*, Springer, v. 32, p. 123–145, 2009. Citado 2 vezes nas páginas 53 e 325.

UPADHYAY, M. K. et al. Utilizing the potential of microorganisms for managing arsenic contamination: A feasible and sustainable approach. *Frontiers in Environmental Science*, Frontiers, v. 6, p. 24, 2018. Citado na página 138.

VALLEDOR, L. et al. Systemic cold stress adaptation of chlamydomonas reinhardtii. *Molecular & Cellular Proteomics*, ASBMB, v. 12, n. 8, p. 2032–2047, 2013. Citado na página 280.

VIA, J. D. et al. Influence of long-term hypoxia exposure on the energy metabolism of solea solea. ii. intermediary metabolism in blood, liver and muscle. *Marine Ecology Progress Series*, JSTOR, p. 17–27, 1994. Citado na página 54.

VOLANT, A. et al. Spatial distribution of eukaryotic communities using high-throughput sequencing along a pollution gradient in the arsenic-rich creek sediments of carnoulès mine, france. *Microbial ecology*, Springer, v. 72, n. 3, p. 608–620, 2016. Citado 3 vezes nas páginas 101, 137 e 282.

WANG, H. et al. Variations of arsenic forms and the role of arsenate reductase in three hydrophytes exposed to different arsenic species. *Ecotoxicology and Environmental Safety*, Elsevier, v. 221, p. 112415, 2021. Citado na página 285.

WANG, P.-H. et al. An interspecies malate–pyruvate shuttle reconciles redox imbalance in an anaerobic microbial community. *The ISME Journal*, Nature Publishing Group UK London, v. 13, n. 4, p. 1042–1055, 2019. Citado na página 273.

WANG, W. et al. Seven-year dynamics of testate amoeba communities driven more by stochastic than deterministic processes in two subtropical reservoirs. *Water Research*, Elsevier, v. 185, p. 116232, 2020. Citado na página 286.

WANG, X. et al. Stress-sensitive protein rac1 and its involvement in neurodevelopmental disorders. *Neural plasticity*, Hindawi, v. 2020, 2020. Citado na página 195.

WANG, X. et al. Pyruvate dehydrogenase kinases (pdks): An overview toward clinical applications. *Bioscience Reports*, Portland Press, v. 41, n. 4, 2021. Citado 2 vezes nas páginas 272 e 283.

WANG, Y. et al. Review of arsenic speciation, toxicity and metabolism in microalgae. *Reviews in Environmental Science and Bio/Technology*, Springer, v. 14, p. 427–451, 2015. Citado na página 160.

WATERHOUSE, R. M. et al. Orthodb: the hierarchical catalog of eukaryotic orthologs in 2011. *Nucleic acids research*, Oxford University Press, v. 39, n. suppl_1, p. D283–D288, 2011. Citado na página 103.

WEN, J. et al. Utility of transcriptome sequencing for phylogenetic inference and character evolution. 2015. Citado na página 224.

WHEATON, W. W.; CHANDEL, N. S. Hypoxia. 2. hypoxia regulates cellular metabolism. *American Journal of Physiology-Cell Physiology*, American Physiological Society Bethesda, MD, v. 300, n. 3, p. C385–C393, 2011. Citado na página 246.

WIEHE, R. S. et al. Endonuclease g promotes mitochondrial genome cleavage and replication. *Oncotarget*, Impact Journals, LLC, v. 9, n. 26, p. 18309, 2018. Citado na página 200.

WOLFE, A. J. The acetate switch. *Microbiology and molecular biology reviews*, Am Soc Microbiol, v. 69, n. 1, p. 12–50, 2005. Citado na página 276.

WOOLBRIGHT, B. L. et al. The role of pyruvate dehydrogenase kinase-4 (pdk4) in bladder cancer and chemoresistance. *Molecular Cancer Therapeutics*, AACR, v. 17, n. 9, p. 2004–2012, 2018. Citado na página 272.

WU, B.; SONG, J.; BEITZ, E. Novel channel enzyme fusion proteins confer arsenate resistance. *Journal of Biological Chemistry*, Elsevier, v. 285, n. 51, p. 40081–40087, 2010. Citado 4 vezes nas páginas 50, 109, 121 e 159.

XIE, N. et al. Nad+ metabolism: pathophysiologic mechanisms and therapeutic potential. *Signal transduction and targeted therapy*, Nature Publishing Group UK London, v. 5, n. 1, p. 227, 2020. Citado 2 vezes nas páginas 244 e 275.

XIE, Z. et al. Cathepsin b in programmed cell death machinery: mechanisms of execution and regulatory pathways. *Cell Death & Disease*, Nature Publishing Group UK London, v. 14, n. 4, p. 255, 2023. Citado na página 200.

YANG, H.-C. et al. Pathways of arsenic uptake and efflux. In: *Current topics in membranes*. [S.l.]: Elsevier, 2012. v. 69, p. 325–358. Citado 3 vezes nas páginas 99, 138 e 159.

YE, J. et al. Crystal structure of the flavoprotein arsh from sinorhizobium meliloti. *FEBS letters*, Elsevier, v. 581, n. 21, p. 3996–4000, 2007. Citado na página 100.

YELLEN, G. Fueling thought: Management of glycolysis and oxidative phosphorylation in neuronal metabolism. *Journal of Cell Biology*, Rockefeller University Press, v. 217, n. 7, p. 2235–2246, 2018. Citado na página 54.

YOSHIDA, Y. et al. De novo assembly and comparative transcriptome analysis of euglena gracilis in response to anaerobic conditions. *BMC genomics*, BioMed Central, v. 17, n. 1, p. 182, 2016. Citado 3 vezes nas páginas 205, 225 e 283.

ZAFAR, S.; AQIL, F.; AHMAD, I. Metal tolerance and biosorption potential of filamentous fungi isolated from metal contaminated agricultural soil. *Bioresource technology*, Elsevier, v. 98, n. 13, p. 2557–2561, 2007. Citado 3 vezes nas páginas 101, 137 e 282.

ZENG, W. et al. Hemerythrin is required for aeromonas hydraphlia to survive in the macrophages of anguilla japonica. *Genet Mol Res*, v. 15, n. 2, 2016. Citado na página 268.

ZHANG, D. et al. Metabolic reprogramming of cancer-associated fibroblasts by idh3θ downregulation. *Cell reports*, Elsevier, v. 10, n. 8, p. 1335–1348, 2015. Citado na página 273.

ZHANG, H.-n. et al. Systematic identification of arsenic-binding proteins reveals that hexokinase-2 is inhibited by arsenic. *Proceedings of the National Academy of Sciences*, National Acad Sciences, v. 112, n. 49, p. 15084–15089, 2015. Citado na página 198.

ZHANG, J.; MARTINOIA, E.; LEE, Y. Vacuolar transporters for cadmium and arsenic in plants and their applications in phytoremediation and crop development. *Plant and Cell Physiology*, Oxford University Press, v. 59, n. 7, p. 1317–1325, 2018. Citado na página 50.

ZHANG, J. et al. Role of ubiquitination in arsenic tolerance in plants. *Trends in Plant Science*, Elsevier, 2023. Citado na página 199.

ZHANG, X. et al. Unraveling the regulation of hepatic gluconeogenesis. *Frontiers in endocrinology*, Frontiers Media SA, v. 9, p. 802, 2019. Citado na página 270.

ZHAO, F. et al. Arsenic uptake and metabolism in plants. *New Phytologist*, Wiley Online Library, v. 181, n. 4, p. 777–794, 2009. Citado na página 50.

ZHENG, J. Energy metabolism of cancer: Glycolysis versus oxidative phosphorylation. *Oncology letters*, Spandidos Publications, v. 4, n. 6, p. 1151–1157, 2012. Citado na página 54.

ZHENG, S. et al. Role and mechanism of actin-related protein 2/3 complex signaling in cancer invasion and metastasis: A review. *Medicine*, Wolters Kluwer, v. 102, n. 14, p. e33158–e33158, 2023. Citado na página 186.

ZIESENISS, A. Hypoxia and the modulation of the actin cytoskeleton–emerging interrelations. *Hypoxia*, Dove Press, v. 2, p. 11, 2014. Citado na página 246.

ZIMORSKI, V. et al. Energy metabolism in anaerobic eukaryotes and earth's late oxygenation. *Free Radical Biology and Medicine*, Elsevier, v. 140, p. 279–294, 2019. Citado na página 205.

ZOU, S.; ZHANG, Q.; GONG, J. Comparative transcriptomics reveals distinct gene expressions of a model ciliated protozoan feeding on bacteria-free medium, digestible, and digestion-resistant bacteria. *Microorganisms*, MDPI, v. 8, n. 4, p. 559, 2020. Citado na página 44.