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PERSPECTIVE

How toxicity drives evolution: past, present and future

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Abstract

The evolutionary context of environmental toxicology and chemistry in the Anthropocene is expanded towards a global perspective through three complementary approaches: (i) environmental toxicity as a mechanism to explain selectivity in mass extinctions with the K-Pg event as a case study; (ii) evidence that certain features of embryonic development could be considered biomarkers of adaptation to specific environmental agents of the evolutionary process, e.g. the transition from the anaerobic to the aerobic metabolism in early embryonic stages versus from the anoxic toward the oxic Earth, and (iii) the capacity to build favorable conditions for life by the collaboration of a population of free-living embryos reducing environmental toxicity and its evolutionary implications from an onto-phylogenetic perspective. Focusing on the future, the article highlights the relevance of environmental toxicology and chemistry for sustainability, to understand the characteristics of eventual extraterrestrial life better, and for space colonization initiatives. The acronym EVOTOX is proposed for environmental toxicology and chemistry studies focusing on evolution, past, present, and future.

Keywords Evolutionary toxicology · Mass Extinction · Adaptation · Onto-phylogenesis · Biomarkers · Astrobiology

Introduction

The study of multi-faceted interactions of living organisms and the environment includes a large number of specializations from molecular to the landscape (Guo et al. 2023; Anderson et al. 1994; Herkovits and Perez Coll 2007; Herkovits et al. 2006a; Franco 2024; Herkovits and Perez Coll, 2003, Suter 2020; Gilbert 2009; Laland and Boogert 2010; Diaz et al. 2022; Tarazona et al. 2024). While biodiversity flourishes in the most favorable conditions for life, our understanding of the limits at which life remains possible has expanded to extreme environmental conditions, from the stratosphere to the ocean depths. LUCA (Last Universal Common Ancestor), the hypothesized most primitive form of life capable of leaving descendants to this day, fascinates us with its extraordinary potential for the current global biodiversity and the many species that became extinct throughout evolution, estimated at more than 99% of all species descended from LUCA. Stressful conditions can be extremely effective in shifting the mean of a trait by imposing directional selection and, therefore, are actively involved in both adaptation and extinction processes. As the number of endangered species and biodiversity loss increases, scientists from different disciplines recognize that the Anthropocene imposes a very intense evolutionary process. The evolutionary theory is gradually enriched by contributions from different disciplines (Laland et al. 2014). In the early 90 s, somatic and heritable effects of environmental genotoxins pointed out the need for an evolutionary approach to ecotoxicology (Bickham and Smolen 1994) while the Anthropocene boundary was crossed by exploring the role of environmental toxicity in the selectivity of a mass extinction event (Herkovits 2001a, b). Employing different approaches, the evolutionary perspective of environmental toxicology and chemistry became of increasing interest. This article uses various approaches and case studies to show the importance of environmental toxicology and chemistry in evolution. It offers new ideas on how these fields can help protect the biosphere and aid in understanding extraterrestrial life and space colonization. The acronym EVOTOX is proposed as a term that includes all evolutionary aspects of ecotoxicology, past, present, and future.

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EVOTOX in the earth

Although toxic effects have been known since antiquity, ecotoxicology began in the second half of the 20th century in response to growing concern about the impact of physical and chemical agents on the ecosystem (Carson 1962). It is broadly recognized that living organisms undergo coevolution in response to changing environmental conditions. Ecotoxicology within the context of the Anthropocene has concentrated on assessing the impact of environmental stressors at all levels of biological organization to establish criteria to safeguard ecosystems and human health. This has expanded our understanding of the complexity of life versus the toxic limits for different species, from mechanisms of acclimation to lethality (Perez Col et al. 1999; Sztrum et al. 2011). At local and regional levels, it was reported that a wide range of species acquired resistance to noxious agents subsequent to the application of pesticides and/or other pollutants (Hawkins et al. 2019 Guo et al. 2023, Castro Echavez and Leal 2021). Highly toxic sites are characterized by the disappearance of sensitive or poorly tolerant species (Herkovits et al. 2006; Otto 2018; Wagner et al. 2021). Moreover, as in other species, toxicants also shape natural human variation in terms of genetic and epigenetic diversity (Bolognesi et al. 2002). Thus, as an increasing number of studies on mechanisms of toxicity became multidisciplinary, different approaches provided information allowing an evolutionary explanation of Ecotox results, with a focus on how toxic substances in the environment affect the evolution of populations (e.g. Bickham and Smolen 1994; Coutellec and Barata 2011; Bickham 2001; Straub et al. 2020 Ford and Le Blanc 2020). Omics methods, including genomics, proteomics, and metabolomics, are increasingly utilized in ecotoxicology to examine the impacts of toxic substances on organisms and ecosystems at a molecular level, alongside their potential for informatics integration (Afshari et al. 2011; Ankley et al. 2006; Ebner 2021). These approaches can pinpoint specific molecules or patterns of molecular alterations that serve as biomarkers for exposure and effects. Furthermore, a deeper understanding of the molecular mechanisms of toxicity may result in more precise and dependable chemical risk assessments (Oziolor et al. 2020) and innovations in remediation and mitigation strategies. From an evolutionary toxicology standpoint, omics helps connect chemical contamination with multigenerational and population-wide impacts across various species (Oziolor et al. 2007; Brady et al. 2017). Based on the complex interrelations between environmental features and living organisms during the Anthropocene, the possibility of exploring the role of toxicity for a better understanding of the whole evolutionary process is illustrated below through three complementary approaches and case studies.

i. **Toxicity and mass extinctions** (Paleoecotoxicology, Herkovits 2001a, b). The evolutionary perspective of Ecotoxicology surpassing the Anthropocene arose in the face of two main questions: (i) Is there a planetary boundary event for biodiversity due to toxicity? and (ii) Can basic concepts from ecotoxicology be applied to better understand the evolutionary process? The mass extinction of the dinosaurs was selected as a case study of a catastrophic event. The chemical stress hypothesis is based on the chemical storm resulting from the asteroid that impacted the Earth (Alvarez et al. 1980) and Deccan Trap volcanic activity (Hernandez 2021) ending the Cretaceous Period. This created a distinct layer in the Earth's rock record, known as the K-Pg boundary. Iridium at the K-Pg boundary is up to 160 times its background crustal abundance, while the asteroid impact would have ejected about 60 times the object's mass into the atmosphere as pulverized materials, an estimated 6.8×10^{18} g of chemicals (Alvarez et al. 1980) that is several orders of magnitude higher than the annual global mine production of well-known toxic substances (Herkovits 2001b). Applying basic concepts from ecotoxicology, such as exposure, bioaccumulation, biomagnification, food, habitat preference, susceptibility to noxious agents, etc., points out the potential mechanisms involved in the selectivity of the mass extinction event (Herkovits 2001a, b). Moreover, in addition to the well-known mechanisms of toxicity produced by noxious agents, such as metabolic, mutagenic, endocrine, neural, immune, and reproductive disruptions, the potential synergistic mechanisms of toxic and infectious agents should be considered. As reported during the COVID-19 pandemic (Herkovits 2023), the high environmental toxicity at the K-Pg event could have triggered a cascade of adverse effects, resulting in increased severity of infectious diseases, providing additional explanation for the selectivity within the catastrophic event. Climate changes e.g. temperature could also modify toxicity (Perez-Coll et al. 1986). Fig. 1 depicts a graphical abstract of the selectivity for dinosaurs as an example within the mass extinction event and basic ecotox data on Ir toxicity

The study of mass extinction based on toxicity (Herkovits 2001a b) represents a first contribution that explores a possible planetary boundary for the biosphere due to toxic agents that to date have not been able to be evaluated within the Anthropocene (Richardson et al. 2023). Paleoecotoxicology, initiated as a contribution to a better understanding of the fossil record, was later applied to regional studies in the Anthropocene (Korosi et al. 2017).

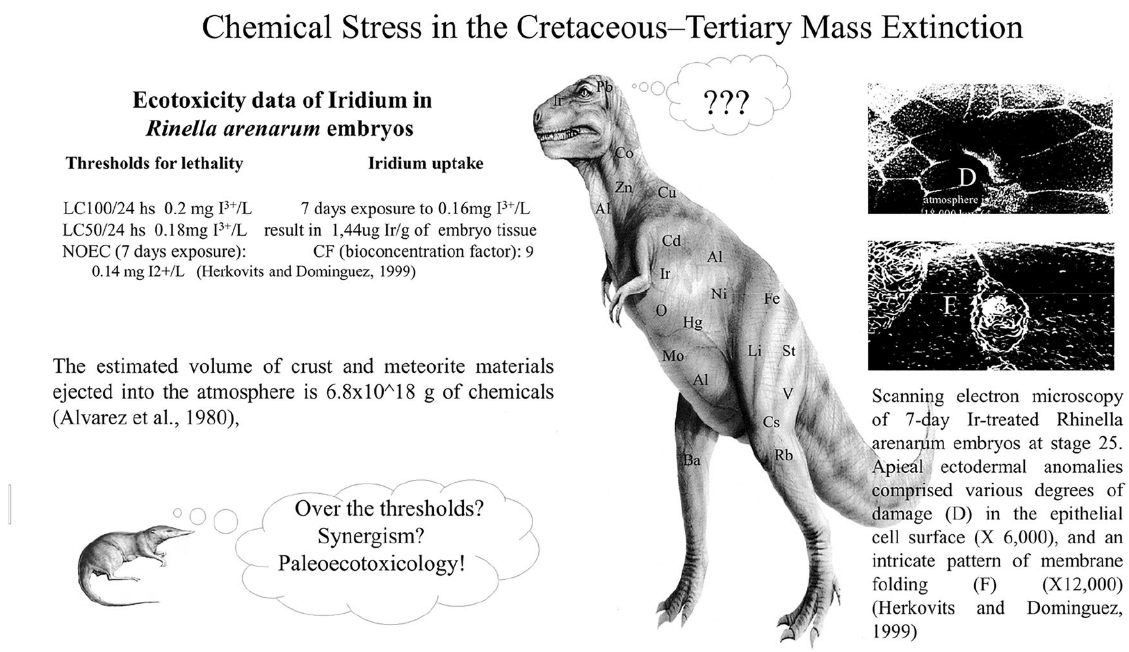

Fig. 1 High bioaccumulation and biomagnification of toxic agents as relevant mechanisms in selective lethality. (Herkovits and Dominguez 2000)

ii. **The record of past environmental features in living organisms** (Evoecotoxicology, Herkovits 2006). Evolutionary-developmental biology (evo-devo) has its origin in comparative embryology in the work of von Baer and Haeckel in the nineteen century, whose "laws" of embryonic divergence and recapitulation were put forward as being generally indicative of phylogeny (von Baer 1828; Haeckel 1886, 1896). A major advance in evo-devo resulted in the discovery of the homeobox genes and the conservation of their pattern of spatiotemporal expression (McGinnis et al. 1984; Scott and Weiner 1984; Scott 2004). Regardless of whether the model system is a hydra segment, a fruit-fly appendage, a budding plant leaf or a human vertebra, all organisms are used for a common molecular phenomenon to explain an organism's body plan (Goodman and Coughlin 2000; De Robertis 2008; Wu et al. 2025; Richardson 2022). The role of environmental signatures within the evo-devo biology field arose from the question of whether specific embryonic features at specific developmental stages could be biomarkers of environmental signatures from the evolutionary process (Herkovits 2006). As a case study, Earth oxygenation was selected as one of the most significant global environmental changes that affected the history of the Earth, initiated about 2.4 Gy ago. In the face of the bio-generated environmental pollutant (oxygen), anaerobes died or restricted themselves to anoxic environments whereas other organisms began using O_2 for metabolic transformation and more efficient energy production. The fact that both vertebrates and invertebrates at early developmental stages are anaerobic (e.g. Barbieri and Legname 1966) and oxygen consumption increases gradually as development advances (Herkovits 2006), could indicate a potentially close correlation between environmental conditions and the evolution of living organisms toward increasing complexity. Thus, anaerobic blastula-like organisms could have existed more than one Gy earlier than registered by undisputed fossil records. As a new dating method, Herkovits (2006) inferred that multicellular organisms flourished over 2 Gy ago, probably even in the Anoxic Earth. Some years after the Evoecotox article was published, the first 2.1 billion-year-old multicellular fossils were reported (El Albani et al. 2010) but without conclusive evidence of a metazoan organism (Anderson et al. 2024). Moreover, the evolutionary origins of how and when the multicellular process first emerged remain elusive (Olivetta et al. 2024).

It can be inferred that as Earth became oxygenated, some organisms gradually developed an increasing aerobic metabolism as is seen during the ontogenesis of vertebrate and invertebrate species (Herkovits 2006). For example, development of amphibians from the egg cell stage until the gastrula stage under anoxic conditions has no ulterior adverse effects, but later, as development advances embryos can survive gradually less time in anoxic conditions before development is

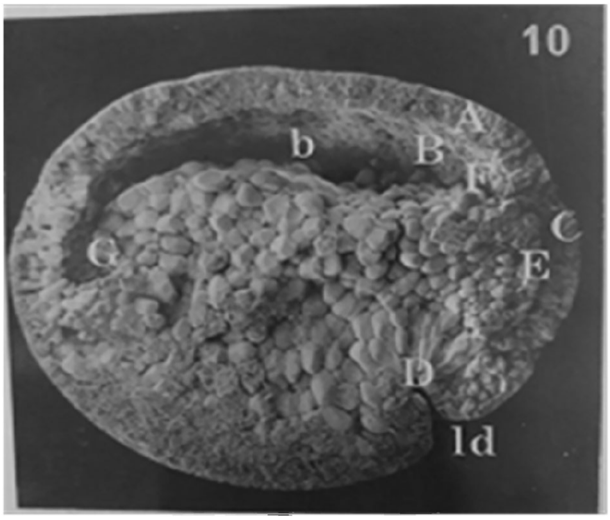

Fig. 2 Sagittal SEM view of a *Rhinella arenarum* early gastrula stage embryo (about 10.000 cells). D cells are the organizers of gastrulation (Herkovits 1978)

Fig. 3 Sagittal SEM view of a *Rhinella arenarum* embryo at neural tube stage. (Herkovits 1978). As embryonic development advances, an increasing oxygen consumption is required for further cell differentiation and morphogenetic processes

arrested, probably due to an insufficient energy supply (Herkovits and D´Eramo, unpublished results). It is noteworthy that the Spemann-Mangold Organizer of embryonic development at the beginning of the amphibian gastrula stage (Fig. 2) is associated with the hypoxia-inducible factor 1α (MacColl Garfinkel et al. 2023), a well-known transcription factor associated with oxygen. Gastrulation is a key event for further advances in onto-phylogeny towards more complex morphogenetic and cell differentiation processes (Fig. 3)

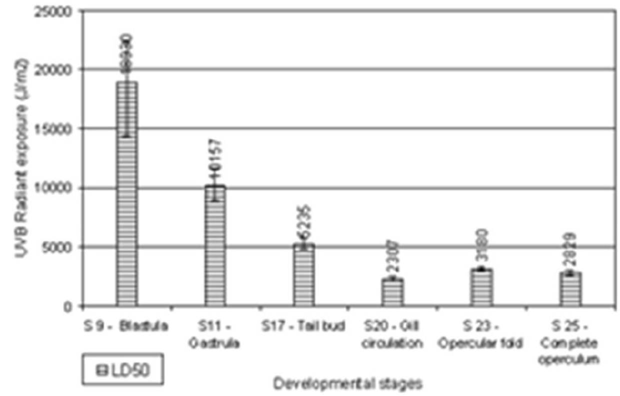

Fig. 4 The very high resistance to UV-B at early embryonic stages correlate with an anoxic Earth (no ozone shelter) and anaerobic metabolism. Conversely, as development advances (Castanaga et al. 2009)

The remarkable, stage-dependent susceptibility to noxious agents (Herkovits et al. 1998; Sztrum et al. 2011) could be considered a biomarker of significant changes in the environmental conditions of living organisms' ancestors at different times of their phylogenesis. For example, before the presence of free oxygen in the atmosphere, no ozone shelter existed, leading to high UV-B exposure in species living in surface water, such as the amphibian embryos ancestors. Coincidentally, amphibian embryos at the blastula stage exhibit the highest resistance to UV-B irradiation (Herkovits et al. 2006b; Castañaga et al. 2009) (Fig. 4) as well as to other noxious agents (e.g. Herkovits et al. 1998; Sztrum et al. 2011). Assuming the high resistance to noxious agents at the blastula stage as a biomarker of environmental signatures, it could reflect harsh environmental conditions that existed during early multicellular life and highlight that subsequent low toxicity and an oxygenated environment were critical for onto-phylogenetic advancements towards diversity in cell differentiation, morphogenesis and therefore biodiversity

iii. **Construction of a Living Environment** (Herkovits et al. 2015). Besides abiotic events shaping environmental features (e.g, Roslin et al. 2021) it is well known that organisms modify various aspects of their environment, eventually destroying what was the habitat of another species or, conversely, providing the conditions for the growth of others. The Anthropocene is an excellent example of global environmental changes with significant adverse effects, including for our species (e.g., Carson 1962). Could the evolutionary process have favored the ability of living beings to generate general conditions beneficial for their existence? It is well known that in the

Fig. 5 Amphibian embryos developing with extreme deformities produced by constraints in the surrounding media (EDE) compared with control embryos (CE). Released from the experimental condition, embryos gradually recover a normal shape, developing into normal larvae and toad (Herkovits 1977)

> presence of toxins, living beings develop a variety of defense mechanisms. This is an expression of their adaptation capacity, resulting in resilience whose magnitude can be evaluated even at the morphological level (Fig. 5, Herkovits 1977).

Since toxicity is a hazard that comes from the outside, it was considered of interest to investigate whether organisms, in addition to the defense mechanisms to reduce the impact of toxicity on their vital functions, actively try to modify the environment to reduce toxicity from the source. In the case of free-living embryos, it could imply the capacity to modify their environment toward more favorable conditions for life. For this study, environmental pH was selected as a fundamental water quality parameter, and mechanism of toxicity. Exposed to toxic acidic environments, free-living embryos collectively contribute to alkalinizing their environment toward neutral pH. This capacity also has beneficial effects in the case of chemicals like aluminum, which exacerbate toxicity by lowering environmental pH (Herkovits et al. 2015). The study highlights an underestimated aspect of potential relevance for species' survival despite toxicity and for the recovery of highly acidic scenarios. It is noteworthy that within an onto-phylogenetic perspective, this discovery allows us to conclude that living organisms have actively collaborated to create and preserve favorable conditions for life since ancient times. The fact that even bacterial interactions include modifying environmental pH (Barrie Johnson 1998) points out the ancient capacity of living organisms to modify environmental parameters. Thus, it can be envisioned that this cooperation at the population level likely coexisted with, and possibly preceded competition, which has been considered the fundamental law of evolution since Darwin. The term "coopetition" is proposed, which implies cooperation between individuals of one or more species to generate favorable conditions for life, alongside competition among the fittest. This study conducted in a petri dish provides support for the concept of the living world as a woven fabric or tapestry (Diaz et al. 2022) and the controversial Gaia hypothesis of a holistic, synergetic system where living things and their environment interact to regulate the conditions for life on Earth (Lovelock and Margulis 1974).

The next aspect of this perspective focuses on the relevance of environmental toxicology and chemistry for successful space exploration and colonization

EVOTOX in the universe: ASTROEVOTOX

Astrobiology, as a multidisciplinary endeavor, has expanded the boundaries of biological investigations into the origin, evolution, and distribution of life on Earth and elsewhere in the Universe (Hallsworth et al. 2021; Mirbahai, Chipman, 2014; Schultz et al. 2023). The prospects of discovering extraterrestrial life and space colonization have garnered increasing interest, especially since the Apollo 11 mission in 1969, which placed the first humans on the Moon. Several countries are actively developing space programs, with one of the most ambitious goals being the establishment of a human colony on the Moon or even Mars. Although the environmental conditions on the Moon are extremely hostile for Earth organisms (Jaumann et al. 2012; Cockell et al. 2024), the Moon's complex structure has revealed many surprises, such as the presence of substantial amounts of underground water and extensive tunnel systems. These features could harbor chemical substances not yet identified, and over billions of years, they could develop significant organizational complexity simply by adhering to thermodynamic laws. Given this potential, refuges on the Moon as well as in other extra-Earth locations could facilitate the survival of both human cells and microorganisms in astronauts' bodies by protecting them from life-threatening factors. Additionally, these refuges could support or facilitate the creation of ecosystems using selected Earth species for specific purposes. One critical condition is that environmental toxicity within a refuge on the Moon or any other extraterrestrial location must remain within toxicity limits compatible with the developing ecosystem and human health. For instance, potential exposure to toxic agents like lunar dust could represent a high health risk (Cain 2010; Loftus et al. 2010).

The history of the Earth's biosphere and the capacity of living forms to adapt to changing and even "extreme" environmental conditions (Shultz et al. 2023) provide clues to understanding that organisms, from microbes to humans, can thrive beyond Earth's conditions (Horneck 1999). The unexpected high resistance and resilience of microbes (Deguchi et al. 2011) and even vertebrate embryos to hyper-acceleration attributable to extreme gravity (Herkovits and Colombo 1981a, b), as well as living organisms' capacity to build favorable conditions for life (Herkovits et al. 2015), point to the potential for selected organisms to flourish in constructed extraterrestrial environments. However, spatial conditions have deleterious effects, such as a reduction in immune competence, harmful changes to the microbiome composition, and their potential increased virulence that could lead to a higher risk of infection (Taylor 2015). Moreover, as mentioned, the potential exposure to toxic agents like lunar dust could pose a significant health risk (Loftus et al. 2010). Considering that even temperature can modify toxicity (Perez Coll et al. 1986), studies on living organisms responding to toxic agents in space conditions could be relevant for the success of extraterrestrial colonization efforts.

In addition to analytical methods and toxicity biomarkers, there are holistic assessments for environmental health toxicity limits (Herkovits et al. 2006a), including possible synergy mechanisms between toxic and infectious agents (Herkovits 2023), necessary as early warnings and for the maintenance of the extraterrestrial ecosystem within toxicity limits that avoid catastrophic consequences. Comparative studies on Earth and under space conditions could address research goals relevant for Astrobiology. From an evolutionary perspective, the approaches and case studies illustrated in this contribution could provide insights for exploring and understanding evolutionary processes in Astrobiology, incorporating an ecotoxicological perspective. Thus, Astroecotox, a merger of astrobiology and ecotoxicology, is proposed as a self-aware scientific endeavor contributing to Astrobiology (Fig. 6).

Whether life on Earth originated through abiogenesis or panspermia, the Universe, populated by billions of celestial bodies, offers potential conditions for life or other highly complex entities. Recent developments in thermodynamics, have shown that structures of increasing complexity could evolve if basic atoms and molecules are available as building blocks (England 2013). Thus, toxicity-based features will be of high priority in understanding alien life conditions as well as environmental conditions sustainable for a long-term space exploration.

Fig. 6 Non-toxic conditions are necessary for different purposes of extraterrestrial colonization

In pursuit of humanity's goal to explore the Universe, Astroecotox could address at least three main objectives: (i) evaluating extraterrestrial agents/environments for their suitability for terrestrial life; (ii) the construction of ecosystems that could eventually sustain humans in extraterrestrial locations; and (iii) understanding the environmental limits of extraterrestrial beings of biological or other complexities, including evolutionary aspects. Ultimately, the advancement of Astroecotox will also enhance our capacity and commitment to environmental and health protection on Earth.

Conclusions

Environmental toxicity due to anthropogenic activities has led to a multidisciplinary understanding of the complex interrelationship between living organisms and their environment. In the present study, starting from the Anthropocene, the evolutionary dimension of ecotoxicology is expanded to the whole evolutionary process through case studies of toxicity as a key parameter in understanding the interrelationship between living organisms and their environment throughout the evolutionary process. The potential for toxicity to trigger a planetary catastrophe was exemplified through the high exposure to and mechanisms of toxicity during the K-Pg mass extinction event. For adaptation, an onto-phylogenetic approach highlights the record of environmental signatures in living species at specific ontogenic stages and their fundamental role in evolution. In this context, the notable changes in susceptibility to harmful agents at different stages of embryonic development could reflect the environmental changes that their ancestors underwent at specific stages of their phylogenesis. Thus, the environmental approach contributes to an integrated view of evolution and development. As a byproduct, a new dating method allowed the prediction that multicellular organisms would flourish before 2 Gy, confirmed later by the fossil record. The construction of a living planet was exemplified by the ability of free-living embryos to modify a toxic environment into one more favorable for life. This discovery completes the circle of global interrelationships between living organisms and their environment, demonstrating that, since ancient times, organisms have actively contributed to creating favorable conditions for life. Combined with the traditional concept of adaptation, this has allowed life to thrive at increasing levels of complexity despite catastrophic events like mass extinctions.

Concerning the future, ecotoxicological management is essential for the sustainability of the biosphere and for our efforts to colonize space and understand potential extra-terrestrial life. The acronym EVOTOX represents the interrelation between living beings and environmental conditions related to toxicity throughout the past, present, and future, encompassing the entire evolutionary process.

Data availability

No datasets were generated or analysed during the current study.

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Compliance with ethical standards

Conflict of interest The author declares no competing interests.

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References

Afshari CA, Hamadeh HK, Bushel PR (2011) The evolution of bioinformatics in toxicology: advancing toxicogenomics Toxicol Sci 120(Suppl 1):S225–S237. https://doi.org/10.1093/toxsci/kfq373

Alvarez LW, Alvarez W, Asaro F, Michel HV (1980) Extraterrestrial cause for the cretaceous-tertiary extinction. Science 208:1095–1108.

Anderson RP, Mughal S, Wedlake GO (2024) Proterozoic microfossils continue to provide new insights into the rise of complex eukaryotic life. R Soc Open Sci. https://doi.org/10.1098/rsos.240154

Anderson S, W Sadinski, L Shugart, P et al (1994) Genetic and molecular ecotoxicology: a research framework. Environ Health Perspect:3–8. https://doi.org/10.1289/ehp.94102s123

Ankley GT, Daston GP, Degitz SJ et al. (2006) Toxicogenomics in regulatory ecotoxicology. Environ Sci Technol 40:4055–4065. https://doi.org/10.1021/es0630184.

Barbieri FD, Legname H (1966) Anaerobiosis in the segmenting eggs of *Bufo arenarum*. Development. https://doi.org/10.1242/dev.15.1.61

Barrie Johnson D (1998) Minireview biodiversity and ecology of acidophilic microorganisms. FMS Microbiol Ecol 27:307–317.

Bickham JW (2001) The four cornerstones of evolutionary toxicology. Ecotoxicology 20:497–5021.

Bickham JW, Smolen MJ (1994) Somatic and heritable effects of environmental genotoxins and the emergence of evolutionary toxicology. Environ Health Perspect 102:25–28.

Bolognesi G, Bacalini MG, Pirazzini C et al. (2002) Evolutionary implications of environmental toxicant exposure. Biomedicines 10:3090. https://doi.org/10.3390/biomedicines10123090.

Brady SP, Monosson E, Matson CW, Bickham JW (2017) Evolutionary toxicology: toward a unified understanding of life's response to toxic chemicals. Evol Appl 10:745–751. https://doi.org/10.1111/eva.12519.

Cain JR (2010) Lunar dust: the hazard and astronaut exposure risks. Earth Moon Planets 107:107–125. https://doi.org/10.1007/s11038-010-9365-0.

Carson R (1962) Silent Spring Published by Houghton Mifflin Company

Castañaga LA, Asorey C, Sandoval MT et al. (2009) Stage dependent teratogenic and lethal effects exerted by ultraviolet B radiation on *Rhinella (Bufo) arenarum* embryos. Environ Toxicol Chem 28:427–433.

Castro Echavez VFL, Leal JCM (2021) Ecotoxicological effect of heavy metals in free-living ciliate protozoa of Lake Maracaibo. J Water Land Dev https://doi.org/10.24425/jwld.2021.139020

Cockell CS, Green DA, Caplin N, et al (2024) BioMoon: a concept for a mission to advance space life sciences and astrobiology on the Moon. Discov Sp. https://doi.org/10.1007/s11038-024-09558-4

Coutellec MA, Barata C (2011) An introduction to evolutionary processes in ecotoxicology. Ecotoxicology 20(3):493–496.

De Robertis EM (2008) Evo-devo: variations on ancestral themes. Cell 132:185–195. https://doi.org/10.1016/j.cell.2008.01.003.

Deguchi S, Shimoshige H, Tsudome M, et al (2011) Microbial growth at hyperaccelerations up to 403,627 × g. Proc Natl Acad Sci. https://doi.org/10.1073/pnas.1018027108

Díaz S, Kattge J, Cornelissen JHC et al. (2022) The global spectrum of plant form and function: enhanced species-level trait dataset. Sci Data 9: 755. https://doi.org/10.1038/s41597-022-01774-9.

Ebner JN (2021) Trends in the application of "omics" to ecotoxicology and stress ecology. Genes 12(10):1481.

El Albani A, Bengtson S, Canfield DE et al. (2010) Large colonial organisms with coordinated growth in oxygenated environments 2.1 Gyr ago. Nature 466:100–104.

England JL (2013) Statistical physics of self-replication. J Chem Phys 139: 121923.

Ford A T, LeBlanc G A (2020) Endocrine disruption in invertebrates: A survey of research progress. Environmental Science Technology 54:13365–13369

Franco ME (2024) Environmental realism in molecular ecotoxicology: key considerations to transition experimental data to ecologically relevant scenarios Ecotoxicology 34 https://doi.org/10.1007/s10646-024-02827-y

Gilbert S F and Epel D (2009) Ecological Developmental Biology: Integrating Epigenetics, Medicine and Evolution. In Integrativeand Comparative Biology. https://doi.org/10.1093/icb/icp106

Goodman CS, Coughlin BC (2000) The evolution of evo-devo biology. Proc Natl Acad Sci USA 97:4424–4425.

Guo L, Qiao X, Haji D et al. (2023) Convergent resistance to GABA receptor neurotoxins through plant–insect coevolution. Nat Ecol Evol 7:1444–1456.

Haeckel, E, 1886. Generelle morphologie der organismen. Georg Reimer, Berlin.

Haeckel, E, 1896. The evolution of man: a popular exposition of the principal points of human ontogeny and phylogeny. Appleton, New York.

Hallsworth, Mancinelli JE, Conley RL et al. (2021) Astrobiology of life on earth. Environ Microbiol 23(7):3335–3344. https://doi.org/10.1111/1462-2920.15499.
Hawkins NJ, Bass C, Dixon A, Neve P (2019) The evolutionary origins of pesticide resistance. Biol Rev Camb Philos Soc 94:135–155.
Herkovits J (1977) Are shape and morphogenesis independent phenomena?. Experientia 33:510–513.
Herkovits J (1978) Génesis y regulación de la forma durante el desarrollo embrionario. Doctoral thesis, Faculty of medicine, University of Buenos Aires
Herkovits J (2001a) Paleoecotoxicology: the impact of chemical and physical stress in the evolutionary process. Environ Health Perspect 109:A564–A566.
Herkovits J (2001b) Paleoecotoxicology: extending environmental toxicology and chemistry to the interpretation of the fossil record. Environ Toxicol Chem 20(8):1623.
Herkovits J (2006) Evoecotoxicology: environmental changes and life features development during the evolutionary process. Environ Health Perspect 114:1139–1142.
Herkovits J, Cardellini P, Pavanati C, Pérez-Col CS (1998) Cadmium uptake and bioaccumulation in *Xenopus laevis* embryos at different developmental stages. Ecotoxicol Environ Saf 39:21–26.
Herkovits J, Castañaga LA, D'Eramo JL, Jourani VP (2015) Living organisms influence on environmental conditions: pH modulation by amphibian embryos versus aluminum toxicity. Chemosphere 139:210–215.
Herkovits J (2023) One health: potential synergy between infectious and toxic agents. The case of COVID-19. In: Castano V, Ansaloni L (ed) Academia medicine, ACADEMI- EDU PUBLISHING Academic, Mexico City, p 1–6
Herkovits J, Colombo L (1981a) Capacidad de recuperación de embriones con deformaciones agudas por la aplicación de fuerzas g durante la neurulación. Medicina 41:650.
Herkovits J, Colombo L (1981b) Capacidad de resistencia de embriones en etapas organogenéticas a fuerzas de 30.000 g. Medicina 41:653–654.
Herkovits J, Domínguez O (2000) Could chemical stress be related to biodiversity loss in the cretaceous-tertiary? 21st SETAC NA Meeting, Abstract Book pp11
Herkovits J, Pérez-Coll CS (2007) Acclimation to low level exposure of copper in Bufo arenarum embryos: linkage of effects to tissue residues. Int J Environ Res Public Health 4:166–172.
Herkovits J, Pérez-Coll CS, Castañaga L, et al (2006b) Los efectos teratogénicos como expresión de calidad ambiental actual y desde una perspectiva evolutiva. In: Herkovits J (ed) En: "Salud Ambiental y Humana: Una visión holística", Publicación SETAC LA, Argentina, pp 88–90
Herkovits J, Pérez-Coll CS (2003) AMPHITOX: A standardized set of toxicity tests employing amphibian embryos. Its potential for customized hazard assessment. In: Linder G, Krest S, Sparling D, Little E (ed) Multiple stressor effects in relation to declining amphibian populations. ASTM Selected Technical, West Conshohocken, PA 19428–2959, pp 46–60
Herkovits J, Rodrigues Capítulo A, Boyle T et al. (2006a) Estudio ecotoxicológico del arroyo Las Conchitas (Buenos Aires). I toxicidad en agua y sedimentos; II parámetros físico-químicos y relevamiento de la biota. In: Herkovits J (ed) En "Salud Ambiental y Humana: Una visión holística", Publicacion SETAC LA, Argentina, pp 50–53
Hernandez A, Nava BA, Black SA et al. (2021) Reconciling early Deccan Traps CO2 outgassing and pre-KPB global climate. Proc Natl Acad Sci 118(14):e2007797118.
Horneck G (1999) Astrobiology studies of microbes in simulated interplanetary space. In: Ehrenfreund, P., Krafft, C., Kochan, H., Pirronello, V. (eds) Laboratory Astrophysics and Space Research. Astrophysics and Space Science Library, vol 236. Springer, Dordrecht. https://doi.org/10.1007/978-94-011-4728-6_26
Jaumann R, Hiesinger H, Anand M et al. (2012) Geology, geochemistry, and geophysics of the Moon: status of current understanding. Planet Space Sci 74:15–41.
Korosi J, Thienpont JR, Smol JP et al. (2017) Paleo-ecotoxicology: what can lake sediments tell us about ecosystem responses to environmental pollutants?. Environ Sci Technol 51:9446–9945.
Laland K, Uller T, Feldman M et al. (2014) Does evolutionary theory need a rethink?. Nature 514:161–164. https://doi.org/10.1038/514161a.
Laland KN, Boogert NJ (2010) Niche construction, co-evolution and biodiversity. Ecol Econ 69:15,731–736.
Loftus DJ, Rask JC, McCrossin CG et al. (2010) The chemical reactivity of lunar dust: from toxicity to astrobiology. Earth Moon Planets 107:95–105. https://doi.org/10.1007/s11038-010-9376-x.
Lovelock JE, Margulis I (1974) Atmospheric homeostasis by and for the biosphere: the gaia hypothesis. Tellus 26:2–10.
MacColl Garfinkel A, Mnatsakanyan N, Patel JH et al. (2023) Mitochondrial leak metabolism induces the spemann-mangold organizer via Hif-1α in xenopus. Dev Cell. https://doi.org/10.1016/j.devcel.2023.08.015
McGinnis W, Levine MS, Hafen E et al. (1984) Conserved DNA sequence in homoeotic genes of the *Drosophila Antennapedia* and bithorax complexes. Nature 308:428–433.
Mirbahai L, Chipman JK (2014) Epigenetic memory of environmental organisms: a reflection of lifetime stressor exposures. Mutat Res Genet Toxicol Environ Mutagen 764–765:10–17.
Olivetta M, Bhickta C, Chiaruttini N et al. (2024) A multicellular developmental program in a close animal relative. Nature 635:382–389. https://doi.org/10.1038/s41586-024-08115-3.
Otto SP (2018) Adaptation, speciation and extinction in the Anthropocene. Proc Biol Sci 285:20182047. https://doi.org/10.1098/rspb.2018.2047.
Oziolor EM, Bickham JW, Matson CW (2007) Evolutionary toxicology in an omics world. Evol Appl 10:752–761. https://doi.org/10.1111/eva.12462.
Oziolor EM, DeSchamphelaere K, Lyon D, Nacci D, Poynton H (2020) Evolutionary toxicology-an Informational tool for chemical regulation?. Environ Toxicol Chem 39(2):257–268.
Perez Coll CS, Herkovits J, Fridman O et al. (1999) Metallothionein induction and cadmium uptake in Bufo arenarum embryos following an acclimation protocol. Environ Pollut 106:443–448.
Pérez-Coll C, Herkovits J, Salibián A (1986) Teratogenic effects of cadmium on *Bufo arenarum* during gastrulation. Experientia 42:1174–1176.
Richardson K, Steffen W, Lucht W et al. (2023) Earth beyond six of nine planetary boundaries. Sci Adv 9(37):eadh2458. https://doi.org/10.1126/sciadv.adh2458.
Richardson MK (2022) Theories, laws, and models in evo-devo. J Exp Zool B Mol Dev Evol 338(1-2):36–61. https://doi.org/10.1002/jez.b.23096.
Roslin T, Antão L, Hällfors M et al. (2021) Phenological shifts of abiotic events, producers and consumers across a continent. Nat Clim Change 11:241–248. https://doi.org/10.1038/s41558-020-00967-7.
Schultz J, dos Santos A, Patel N et al. (2023) Life on the edge: bioprospecting extremophiles for astrobiology. J Indian Inst Sci 103:721–737. https://doi.org/10.1007/s41745-023-00382-9.
Scott MP, Weiner AJ (1984) Structural relationships among genes that control development: sequence homology between the Antennapedia, Ultrabithorax, and fushi tarazu loci of Drosophila. Proc Natl Acad Sci 81:4115–4119.
Scott RJ (2004) Embryology, epigenesis and evolution. Cambridge University Press

Straub L, Strobl V, Neumann P (2020) The need for an evolutionary approach to ecotoxicology. Nat Ecol Evol 4, 895. https://doi.org/10.1038/s41559-020-1194-6

Suter GWII (2020) Ecological risk assessment. CRC Press

Sztrum AA, D'Eramo JL, Herkovits J (2011) Nickel toxicity in embryos and larvae of the South American toad: effects on cell differentiation, morphogenesis, and oxygen consumption. Environ Toxicol Chem 30:1146–1152.

Tarazona JV, Alba-Gonzalez M, Bedo C et al. (2024) A conceptual framework for landscape-based environmental risk assessment (ERA) of pesticides. Environ Int 91: 108999. https://doi.org/10.1016/j.envint.2024.108999.

Taylor PW (2015) Impact of space flight on bacterial virulence and antibiotic susceptibility. Infect Drug Resist 30(8):249–262. https://doi.org/10.2147/IDR.S67275.

Von Baer KE (1828) Uber entwicklungsgeschichte der tiere: beobachtung und reflection. Königsberg: Bornträger

Wagner DL, Grames EM, Forister ML et al. (2021) Insect decline in the Anthropocene: Death by a thousand cuts. Proc Natl Acad Sci USA 118:e2023989118. https://doi.org/10.1073/pnas.2023989118.

Wu H, Zhang R, Niklas KJ et al. (2025) Multiplexed transcriptomic analyzes of the plant embryonic hourglass. Nat Commun 16: 802. https://doi.org/10.1038/s41467-024-55803-9.