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Microbes and Society*

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"The task is not so much to see what no one has seen, but to think what nobody has thought about that which everyone sees"

Erwin Schrödinger

Resum

El món microbià es compon de moltes espècies que pertanyen a grups molt diversos. La majoria dels microbis són commensals inofensius i molts d'altres són esencials en el desenvolupament i manteniment de la vida i dels ecosistemes. Cal considerar processos com ara el reciclatge de la matèria orgànica, la mineralització, per la qual els bacteris retornen a l'atmosfera els gasos necessaris per a la vida, o la fixació de nitrogen i carboni convertint aquests gasos en formes metabolitzables pels nostres organismes. També hi ha microorganismes patògens que, desafortunadament, són els més "famosos" ciutadans d'aquesta comunitat. La forta perspectiva antropocèntrica imperant en bona part de la història té a veure amb aquesta consideració hostil vers els microbis. En aquest article comentem la interacció microbis i societat esmentant el potencial humà per modificar la vida i controlar els ecosistemes naturals trencant sovint les pautes de l'evolució per causa d'aquestes modificacions. La conseqüència del ràpid creixement demogràfic, es relaciona directament amb les malalties emergents i un augment de les infeccions nosocomials. A la vegada, noves situacions socials i polítiques indueixen fenòmens preocupants com el bioterrorisme. Els efectes indesitjables dels microorganismes patògens i la seva utilització com a instruments perjudicials, no poden amagar els avantatges de convertir-los en aliats quan es coneixen les seves utilitats.

Paraules clau: biosfera, biotecnologia, malalties emergents, bioterrorisme, activitat microbiana

Abstract

The microbial world is composed of many species belonging to very diverse groups. Most microbes are harmless commensals, while many others are essential for the development and maintenance of life and a wide range of ecosystems. Processes such as the decomposition of organic matter, mineralization, the return to the atmosphere of gases needed by various life forms for nitrogen and carbon fixation, and the conversion of those gases into forms that can be metabolized by other organisms are undertaken by microorganisms. There are also pathogenic microorganisms that, unfortunately, are the "most famous citizens" of this community. The dominant anthropocentric view during large periods of history has been responsible for our hostility towards microbial life. In this paper, we discuss the interaction between microbes and society, the human potential to modify life and control natural ecosystems, and the frequent interruption of evolution that results from these modifications. The rapid growth of the human population has led to the emergence of several new diseases and an increased incidence of nosocomial infections. At the same time, current sociopolitical conditions have made bioterrorism an issue of very real concern. Nonetheless, the harmful effects of pathogenic microorganisms and their perverse use are not reason to forget their benefits and usefulness.

Keywords: biosphere, biotechnology, emerging diseases, bioterrorism, microbial activity

Our two protagonists –arrogant, all-powerful humans with the world at their feet and their formidable technology, on the one hand, and the humble, tiny, and mostly unknown microorganism, on the other– form part of the biosphere, that dense and intricate layer of living creatures and inanimate matter. Despite their different roles, humans and microorganisms are intimately and inevitably related, and they share a large number of characteristics. In this article, we will not discuss the relationship between one microbial species and another. Instead, we consider the relationship between a great number of very diverse species, microbes, and a single species, *Homo sapiens*– which, with our "typical modesty" we named ourselves. It

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should be pointed out that because I, as the author, and you, as the reader, belong to that group, our discussion will be inevitably biased in our favor.

This anthropocentric view –in which humans are the measure of all things– is unavoidable but, too often, it prevents us from understanding properly the rest of the biosphere. Biologists are continuously under pressure to abstract the phenomena they study, i.e., to observe without the ideological burden of anthropocentricity. Bergson summarized this difficulty by saying: "Intelligence is characterized by its natural inability to understand life". However, as difficult as it might be, we should continue trying to observe the biosphere from other points of view. In this article, I will take the side of microorganisms, and attempt to speak for them, since besides being very small and incapable of making decisions, they lack any ability of dialogue and thus cannot explain or justify themselves.

Microorganisms do not constitute a single species; rather, they account for an enormous amount of biodiversity. For one, there are prokaryotic organisms –bacteria and archaebacteria. These are generally simple and single-celled, without specialized organelles or a nucleus and with a limited number of small ribosomes. Eukaryotic microorganisms, such as algae, fungi, and microscopic protozoa, by contrast, have complex cells containing specialized organelles, a nucleus with chromosomes that divides by mitosis, and an extensive network of large ribosomes. To be prokaryotic vs. eukaryotic is possibly the largest evolutionary discontinuity among living organisms.

There are also viruses, which can be defined as microorganisms lacking cellular organization; they consist only of proteins and only one type of nucleic acid. Finally, there are "forms" that can hardly be considered as complete living beings; for example, viroids comprise only short chains of RNA that are capable of replicating themselves in certain hosts, mostly plants, and only under certain conditions; and prions, which appear to be infective proteins.

Common features in the taxonomic spectrum of microorganisms

Among their many shared characteristics, microorganisms have in common their small size. No one has ever seen a bacterium, let alone a virus, with the unaided eye. Indeed, microorganisms are so small and their living matter is so hydrated that even under the microscope they cannot be seen. Instead, they must first be heat-fixed and then dyed with several acids, dyes, and/or stains to overcome the low-level contrast of their biological structures, which do not produce differences in wavelength or in refractive index. Thus, what we ultimately observe are dead cells, whose original aspect has been altered due to fixation and staining. This explains, at least in part, why in the early days of microbiology it was not an easy task to understand microbial life forms.

The discovery of microorganisms was the consequence of two circumstances: (1) the development of techniques such as high-resolution compound microscopes, e.g., the one produced by Abbe and Zeiss in 1872; (2) the talent and ability of the great men at the other end of the microscope, e.g., Pasteur and Koch, who worked without prejudice in applying the scientific method.

The small size of microorganisms bestows upon them several important characteristics that explain their ecological roles and their enormous number of applications. Small size, in this case, generally unicellular or just a few cells, implies a high surface to volume ratio, and thus a high rate of flux, rapid metabolism, and rapid growth. Furthermore, the metabolism of bacteria in particular is not only fast but also extraordinarily diverse. Bacteria are able to carry out processes of synthesis and degradation using a wide range of metabolic pathways and substrates, especially when obtaining energy anaerobically. They also use very distinct pathways in what is known as secondary metabolism, in which rare molecules are synthesized and degraded.

Another characteristic of microbes is their simple genetics and their capacity to survive in "extreme" environments–again, an anthropocentric concept, since these environments are extreme for us humans. Extreme environments are characterized by high pressures and/or temperatures, frozen areas, high salinity, high exposure to sunlight, low concentrations of oxygen, very low or very high pH, etc.

In summary, the small size of microorganisms allows them to grow on almost any substrate and to produce numerous unique molecules. This, together with their simple genetic make-up, confers upon microorganisms an almost inexhaustible biotechnological potential, which humans have exploited empirically since their own beginnings. More importantly, these properties are responsible for the essential role of microbial life in the biosphere. Life would not be possible without microorganisms. Thus, in the following sections, we consider some of the functions of microbes.

Evolutionary role of microorganisms in the biosphere

Microorganisms are capable of decomposing the organic matter of dead plants and animals. Without this ability, the Earth would not only pile up with those corpses, which would quickly occupy all the available space, but there would be an inevitable exhaustion of the food, water, and gases necessary for life. Through processes such as mineralization, microorganisms, mainly bacteria, return to the atmosphere some of the essential gases that life has previously taken from it, such as oxygen, which is required by organisms that carry out aerobic respiration. Nitrogen, carbon dioxide, and several other gases are also recovered, thereby also contributing to maintaining the equilibriums of gases in the air. In addition, some microorganims are able to carry out nitrogen and carbon fixation, in which these gases are converted to forms of carbon or nitrogen that can be metabolized by other organisms. Perhaps the best-known example is nitrogen fixation, in which the absorbable form of this element enriches the soil and thus is critically important for its fertility. The contribution of phytoplankton to the food web in their role as photosynthetic organisms in anoxic and oxic environments is another example of how microorganisms maintain the biosphere. These and other "beneficial actions" of microorganisms are generally unknown to human society, which lives thanks to the efforts of these minute beings.

Living with microorganisms

Human beings are surrounded by microorganisms–there are millions of them all over our body (skin, nose, mouth, pharynx, outer ear, intestine, etc.). Many are simple, harmless commensals, and the majority are beneficial symbionts that protect us from pathogen colonization, synthesize vitamins, and contribute to proper functioning of the intestine. They are known as microbiota or the body's normal biota.

Other microorganisms bear special properties, such as recognition molecules, lytic enzymes, and toxic compounds, that allow them to penetrate discontinuous areas in the epithelium or mucous membranes, while others enter by means of a vector, such as ticks or fleas. Regardless of the mode of entry, once inside the body, these pathogenic microorganisms may overcome our powerful defense mechanisms, multiply, and release their enzymes, toxins, and molecules, thereby causing infectious disease. Virulence factors are what make a microorganism pathogenic. Frequently, such factors are very readily detectable, e.g., in the case of toxin release (tetanus, diphteria, staphylococcus), lytic enzymes (proteases, lipases, DNases, hemolysins), or antiphagocytic capsules. Sometimes, however, the mechanisms are so subtle that it is difficult to understand what differentiates a pathogen from its close, nonpathogenic microbial relative, which is perhaps even from the same species. Explaining recognition at a molecular level continues to be one of the challenges in identifying, understanding, and controlling infectious diseases.

Both humans and bacteria participate in life's great symphony, but the important difference is that only humans, with their capacity for reasoning (and, unfortunately, reasoning is not the same as being reasonable), is able to read the score and modify it through science and technology. Humans participate in natural ecosystems and control many of them, often disrupting the evolutionary guidelines followed by the rest of life. It could be argued that this behavior forms part of our own evolution.

Thanks to human intelligence and through science and technology, we have been able to produce great achievements. Our life has been spectacularly transformed by progress in medicine and pharmacology, agriculture, transport, and communications. For many of us, machines appliances, computers, cars, airplanes, etc., have reduced much of the work of daily life and provide us with more leisure time. Thus, life expectancy –a good index of the quality of life– has almost doubled in the occidental world during the last century (from 40 to 80 years, approximately). To paraphrase Carl Sagan: "If you're dead its unlikely that you are having a good time".

Microorganisms are not foreign to these processes. They have always been employed to improve the quality of life, to the extent that biotechnology can be considered the world's second oldest profession. Humans first used microorganisms empirically; that is, without really knowing what was responsible for processes such as the production of bread, wine, and beer, which go back to biblical times. The presence of microorganims, especially in food, was also empirically avoided through preservation techniques including salt, ice, syrups, and brines.

Currently, as a consequence of advances in molecular biology, along with a better understanding of nucleic acids and enzymes, microorganisms have become the main tool for genetic engineering –the basis of modern biotechnology– since they constitute the best known source of genetic novelty, in addition to the aforementioned properties of versatility, simple genetics, and ease of use. Microorganims have been essential to new developments, such as the synthesis of new medicines, mining, and agriculture.

But, along with these achievements, humans have profoundly altered a large number of ecosystems, through wars, overpopulation, and poverty. Never have the philosopher's words been more accurate: *Homo hominis lupus* (man as a wolf to man). Destruction of the environment is reflected in a series of relatively recent events, including the progressive weakening of the ozone layer, global warming, species extinction, acid rain, and the threats posed by nuclear, chemical, and biological weapons, and toxic waste. These events have either directly or indirectly affected the biosphere and therefore endangered life on Earth. Moreover, perhaps most importantly, rapid population growth has led to major consequences regarding human health, in the form of emerging diseases, nosocomial infections, and the social unrest that has given rise to the threat of bioterrorism.

Emerging diseases

Despite having dominated planet Earth, including its plant and animal inhabitants, humans have failed to control the smallest forms of life. For decades, humanity was confident that science had solved the threat of infectious diseases, given the success of antibiotics, vaccines, health campaigns, etc., against smallpox, polio, and whooping cough. These achievements were reflected statistically: from 1900 to 1982, there was an uninterrupted decrease in mortality due to infectious diseases. However, this tendency ended in 1982, due, among other reasons, to AIDS and its global expansion, the resurgence of tuberculosis, and the appearance of new epidemics, including hantavirus, hepatitis C and E, Ebola virus, Lyme's disease, cryptosporidiosis, or the fearsome *Escherichia coli* strain, *E. coli* O157;H7.

In the UK, a fatal brain disease, (a variant of Creutzfeldt-Jakob disease) transmitted through animal meat and known as "mad-cow disease" was responsible for a number of deaths of several, mostly young, people. Very recently, bird flu, which previously had never affected humans, killed several people in Asia, and the disease now threatens Europe, creating a climate of fear and uncertainty.

Humans will always be confronted with and should always be on guard for the appearance of new infectious diseases and the resurgence of old and supposedly conquered ones, such as tuberculosis, dengue haemorrhagic fever, and yellow fever.

The Centers for Disease Control and Prevention (CDC), in Atlanta, has identified several "new, emerging, or drug resistant" diseases that have resulted from human social and economic development, including the following aspects:

- Population growth together with massive mobility and urbanization
- An increase in the number of intercontinental flights and commerce-related transport
- The invasion of virgin habitats that are reservoirs to carrier insects and animals
- Increases in drug resistance
- Immunosuppressant therapies
- Climate and ecology changes
- Changes in human behavior (sexual practices, drug use, eating habits, etc.)
- Globalization of both food processing and the food supply

Many of the diseases pointed out by the CDC can be considered as zoonotic, i.e., animal diseases that occasionally infect humans, but person to person infection is rare. Infection is generally produced by consumption of contaminated meat or animal food products (brucellosis, listeriosis). Other possible entryways are respiratory (most cases of tuberculosis, psittacosis, pulmonary anthrax); skin discontinuities due to scratches, wounds, or bruises (cutaneous anthrax); or animal bites (plagues). Such diseases have generally been occupational –with high-risk groups comprising butchers, hunters, shepherds, veterinarians, and furriers– and very limited in its transmission from person to person. Moreover, the symptoms of a zoonotic disease can be different in humans than in animals, unless the entry route of the microorganism is the same. Nowadays, what has become worrisome is that the interspecific barrier limiting human infection seems to have become more fragile, placing the entire population at significant risk.

Nosocomial infections

Due to their direct consequences on patient health, the high costs of their control, and the logistic difficulties in limiting their spread, nosocomial infections have been the cause for alarm at many hospitals and medical centers. Given the nature of the infections, hospital personnel, despite having to take obvious precautions, are less susceptible to them. Sir Frank MacFarlane Burnet in his *Natural History of Infectious Diseases* wrote: "Hospitals were historically created as places where sick people could be gathered in order for wise doctors to study their illnesses and to receive the best treatment of the time. Reality turned out to be very different and hospitals became famous for septic disease and 'hospital fevers'. During the 18th and the beginning of the 19th century, the admission to a hospital in a European city was almost equivalent to a death sentence."

Nowadays, despite some imperfections, hospitals come close to fulfilling the original intention with which they were created, i.e., a place where competent professionals study the diseases and treat the patients. Nevertheless, they are not exempt of risks, and one should only be admitted when necessary and accept discharge as early as possible. Nosocomial infections are not caused by primary pathogens, which are not able to infect most normally healthy individuals. Instead, they are the products of secondary or opportunistic pathogens capable of producing infections in individuals whose natural defenses are weak due to age (children and elderly people), immunosuppression (i.e. persons treated with radiation or immunosuppressor drugs, e.g., cancer patients, transplant patients, or those suffering from AIDS), or following surgery or trauma, especially when associated with a great loss of blood, as in car accidents.

When such immunocompromised patients collectively reside in restricted spaces (hospital rooms), they are convenient targets for opportunistic pathogens. The infections caused by these agents tend to be serious, since besides the weakened state of the patient, they are frequently caused by microorganisms that have developed multiple resistances to commonly used antibiotics; this group includes bacteria such as *Pseudomonas* spp., *Serratia* spp., and different viruses or fungi, such as *Aspergillus* ssp. or *Candida* ssp.

Bioterrorism

Finally, in this brief survey of the negative effects of microorganisms in response to the uncontrolled activities of human societies, bioterrorism is a topic of current importance. The CDC defines bioterrorism as the "threatening or deliberate use of viruses, bacteria, fungi or toxins of living organisms to produce death or disease in humans, animals or plants". Bioterrorism agents include "traditional" ones, such as *Bacillus anthracis*, *Brucella suis*, *Francisella tularensis*, *Yersinia pestis*, and *Coxiella burnetii*, as well as newer ones, such as HIV, *Salmonella typhi*, *Vibrio cholerae*, and the *Ebola* virus. In addition, also botulism, cholera, diphtheria, ricin and tetrodotoxin are highly toxic to humans. Recent examples of the use of biological warfare and bioterrorism are the Iraq-Iran war and the anthrax attacks in the USA in 2001.

What are possible measures against bioterrorism? The development of vaccines for the prophylaxis of risk groups, antidotes and products that allow rapid detection and identification of bioterrorism agents, careful food protection, and adequate and immediate medical attention. But, given the menacing situation raised by these threats, it is unclear whether any of these strategies will ultimately be effective.

Many scientists feel that our industrial civilization constitutes an explosive trap, that there is a real and likely danger if humans continue to pursue their activities without considering the environmental consequences. Others say that there is not sufficient cause for worry, that nothing has been proven, and that the environment will preserve itself. In any event, they trust that humanity, which caused the problems, will have the methods to solve them as well. With regards to this, a scientist as rigorous as Margalef, said: "There is nothing new under the sun and man is only putting pressure, according to directions already evident, on strains that made up the pre-human biosphere."

In any case, some of the potential risks are serious enough that it can only be considered prudent to confront the possibility, as small as it may be, the environmental threat due to human behavior poses an extreme danger. If the threat is real, the questions that follow are: Is the threat reversible or can it be neutralized, or have we already gone too far? There is also the problem of defining the priorities for developed vs. developing countries. In developing countries there is not the extreme conflict between growth and quality of life. Economic growth is essential to preserve life and to solve some of the social problems that plague these countries. Even if a conflict between growth and its environmental consequences arises, there is no reason why poor countries should choose between the two in the same way as rich countries.

The consensus reached by many scientists is that the solution will come through the maintenance of development and with it, technological development. It is also understood that these are global problems and should be dealt with globally. Solutions must be arrived at through processes, such as international meetings and agreements, and with the support of international institutions, such as the United Nations, UNESCO, the World Back, and the World Health Organization (WHO).

A serious drawback to seemingly logical approach is that most of these institutions are not democratic in their composition and thus their decisions are biased in favor of the more powerful countries. Economists also raise the issue of the failure of globalization, implying that the market model has changed such that economic models which seem to have worked well in the 1950s and 1960s are now obsolete. Hence, a change in economic theory is needed to adapt to the new developments and it should be followed by a reorganization of international organizations that is consistent with current perspectives.

According to supporters of sustainable development, who also advocate globalization, conservation of the environment is essential to continued economic development. Thus, an environmental approach could be that suggested by L. Bof: “What was the indisputable concept of the world? That everything should revolve around the idea of progress and that this progress moves between two infinites: the infinite of Earth’s resources and the infinite of the future. It was thought that the Earth was never ending in its resources and that we could make progress indefinitely in the direction of the future.

But these two infinites are an illusion. The conscience of crisis recognizes that resources have limits, since not all of them are renewable; that indefinite growth towards the future is impossible because we cannot universalize the model of development for everyone and forever”. “Ecology has abandoned its first stage, in the form of the green movement or the conservation and protection of endangered species, and has become a radical criticism of the civilization model we are building, which is highly energy consuming and disrupting to all systems”.

A different approach to the topic is given, for example, by the Oxford economist Wilfred Beckerman. “During the last decade the environmentalist movement has renewed their attacks to the convenience of economic growth and has redoubled its call to adopt drastic measures in order to avoid an environmental catastrophe. One of the most important developments has been that of the supposed long-term effects of global warming, although the damage to the ozone layer or the apparent loss of biodiversity have also played a role. These are threats which have taken the environmentalist movement to adopt the precaution principle.

Together with the ancient myth that we are going to use up the reservoirs of limited resources, they petition that we should only pretend a sustainable development.

The continuous plea of these two clichés only manages to pressure governments to employ ineffective and expensive policies to regulate the environment, which are frequently designed in a rush and suppose an unjustified intervention in the market’s functioning.” In debating priorities, there is a phrase that serves Beckerman as an introduction: “Poverty is generally the environment’s worst enemy”. “The environment’s ingredients which are of vital interest to thousands of millions of people in developing countries are not those which are in the public’s eye, such as global warming, the damage to the ozone layer or the extinction of the white-headed bald eagle (*Haliaetus leucocephalus*) but the lack of drinking water, hygiene or the poor quality of air in the cities [...] The message: if a reasonable access to drinking water, an adequate hygiene and an acceptable urban air is desired, one has to become rich.

This does not mean that for the world as a whole, or for future generations, other ingredients from the environment (biodiversity, soil erosion, deforestation or pollution of the atmosphere and the oceans) are not considered as important”. Thus, it is clear that all these environmental problems are so complex –socially, economically, politically, and culturally– that they are difficult to properly comprehend, since all sorts of arguments are involved. But the real problems are there and many scientists are dedicated to trying to solve them. Genetic engineers and biotechnologists have met with some success in their attempts to curb pollution, and many of the solutions have involved the use of microorganims. For example, the derivative effects from pesticides and the elimination of non-degradable organic residues from oil spills constitute some of the most important pollution problems that can be tackled with microorganisms able to metabolize the toxic compounds, converting them in the process to nontoxic ones.

Conclusions

Microorganisms, mainly bacteria, are capable of recycling the all or almost all of the natural organic products and the majority of synthetic products manufactured by humans. This ability is essential to life on Earth, since it maintains the atmosphere’s composition and, at the same time, enriches the soil with components needed for plant growth.

Nonetheless, microorganisms cannot metabolize so-called recalcitrant compounds, among which are many pesticides, construction materials of polymeric nature, oil components, and a multitude of plastics commonly used in containers, bags, etc. These and other products contaminate many ecosystems, such as reservoirs, lakes, and even oceans, with accompanying effects on the local flora and fauna and the deterioration of recreational zones, ports, beaches, etc.

Microbial solutions to the problem of recalcitrant compounds will come from several directions. In the case of recalcitrant pesticides, the feasibility of staged degradation through co-metabolism has been studied extensively. An excellent alternative is the use of biological pesticides. A crystallized protein formed in the interior of the spores of *Bacillus thuringiensis* has been isolated and successfully used as a pesticide. This protein has been effectively used in a variety of applications; for example, it destroys caterpillars that affect pine forests, and has no side effects on the environment.

With regards to plastics, the best solution is obtaining –with the help of biotechnology– biodegradable plastics, such as poly hydroxy butyrate (PHB), which is produced by numerous species of bacteria. PHB and other polymers could substitute for synthetic-based plastics, which are of slow or null degradability. However, biodegradable plastics are an expensive alternative, mostly because their large-scale manufacture has not been investigated. Only a few firms with an interest for the environment and whose products are normally expensive, such as those of the cosmetics industry, use them. The prohibition of non-biodegradable packaging would encourage the development of biotechnological products and lead to their progressive reduction in cost.

As for oil spills, microorganisms with a capacity to degrade a wide range of hydrocarbons, with the aid of plasmid-encoded enzymes, has been isolated. Generally, each species of microorganism only degrades a certain type of hydrocarbon (short– or long-chain, saturated, or unsaturated, aromatic, etc.); thus, it has been difficult to obtain a chimeric individual with the ability to degrade multiple types. However, considerable progress has been made. Other possible environmental aids from the field of biotechnology are related to agriculture. Resistance genes to low temperature or high salinity can be transferred to crops, considerably increasing the amount of arable land.

These are but a few examples of the applications of microorganisms to support regenerative measures for the biosphere. But there are many more potential areas of practical application: health (obtaining insulin or growth hormone), industry (substitution of petrochemical processes for biotechnological ones), the food industry, etc.

It is obvious that the use of microorganisms as allies has not been sufficiently taken advantage of. Biotechnology has never enjoyed the financial support that defense or space programs have, and therefore progress has been slower than in these other areas. But these tiny, humble and unselfish workers are there, waiting for us proud humans to turn to them for help. Surely they will not disappoint us.

I would like to finish this contribution with the words of Carl Sagan, who said: “No species has its stay in this planet guaranteed. We have been here for no more than a million years, and are the first species which has conceived the means for self-destruction. We are a rare and precious species because we are capable of reflection and have the privilege of influencing and maybe even controlling our future. I think we have the duty to fight for life on Earth and not only for our own benefit, but for that of all those, human or not, who arrived before us and to who we are obliged, as well as that of those who, if we are sensible enough will come later. There is no cause more urgent and no effort more just than to protect the future of our species.”

About the author

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