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Perspective

Will “Air Eutrophication” Increase the Risk of Ecological Threat to Public Health?

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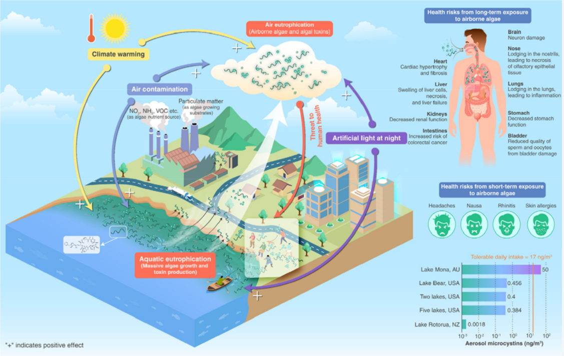

ABSTRACT: Aquatic eutrophication, often with anthropogenic causes, facilitates blooms of cyanobacteria including cyanotoxin producing species, which profoundly impact aquatic ecosystems and human health. An emerging concern is that aquatic eutrophication may interact with other environmental changes and thereby lead to unexpected cascading effects on terrestrial systems. Here, we synthesize recent evidence showing the possibility that accelerating eutrophication will spill over from aquatic ecosystems to the atmosphere via “air eutrophication”, a novel concept that refers to a process promoting the growth of airborne algae, some of them with the capacity to produce toxic compounds for humans and other organisms. Being catalyzed by various anthropogenic forcings—including aquatic eutrophication, climate warming, air contamination, and artificial light at night—accelerated air eutrophication may be expected in the future, posing a potentially increasing risk of threat to public health and the environment. So far knowledge of this topic is sparse, and we therefore consider air eutrophication a potentially important research field and propose an agenda of cross-discipline research. As a contribution, we have calculated a tolerable daily intake of 17 ng m^{-3} day^{-1} for the nasal intake of microcystins by humans.

KEYWORDS: *air eutrophication, airborne algae, microcystins, public health*

AQUATIC EUTROPHICATION, CYANOTOXINS, AND THEIR HEALTH IMPACTS

The great acceleration of the Anthropocene leaves severe imprints on our biosphere.[1,2] Aquatic eutrophication induced by excessive inputs of nutrients (e.g., nitrogen and phosphorus) is among the most conspicuous of the anthropogenic forcings.[3,4] Thus, eutrophication has profoundly impacted aquatic ecosystems and societies and led to, i.a., water quality deterioration, biodiversity loss, and human health problems caused by toxins produced by harmful algal blooms. This has resulted in declines of various ecosystem services,[5,6] which compromises the UN’s Sustainable Development Goals. Cyanobacteria can produce a variety of toxins called cyanotoxins, such as microcystin (MC), which are detrimental and even lethal to invertebrates, fish, birds, and mammals[7,8] (see more in Chart 1). Microcystin-leucine-arginine (MC-LR) is one of the most toxic and common microcystin variants.[9] For humans, oral and dermal contact with water containing high concentrations of cyanobacterial toxins can lead to hepatic dysfunction and other digestive maladies.[10] In 1996, contamination of water supplies with cyanotoxins resulted in the death of more than 60 people in the hemodialysis unit in Caruaru, North-East Brazil.[11] To protect public health, the World Health Organization has proposed a guideline value of MC-LR below 1 $\mu g\ L^{-1}$ in drinking water.[12]

Another additional concern is that eutrophication may interact with other anthropogenic forcings and thereby have led to unexpected cascading environmental changes such as a spillover effect of aquatic eutrophication to terrestrial systems catalyzed by climate change. Promoted by increased frequency and intensity of hot-dry climate extremes, massive growth of cyanobacteria in waters elevates cyanotoxins to extreme levels that may be lethal to terrestrial megafauna. Examples of this are

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Chart 1. Types of Cyanotoxins and Toxicity of Microcystins

I. Cyanotoxins can be classified into various types according to their modes of action, target cells, and organs as hepatotoxins (the most frequently encountered), neurotoxins, dermatotoxins, and cytotoxins.

II. The symptoms of cyanotoxin poisoning include skin irritation, stomach aches, vomiting, nausea, diarrhea, fever, sore throat, and headache.

III. Microcystins, the best-known group of cyanobacterial toxins, mainly cause liver damage but may also entail neurotoxicity, reproductive toxicity, genotoxicity, and potential carcinogenicity.

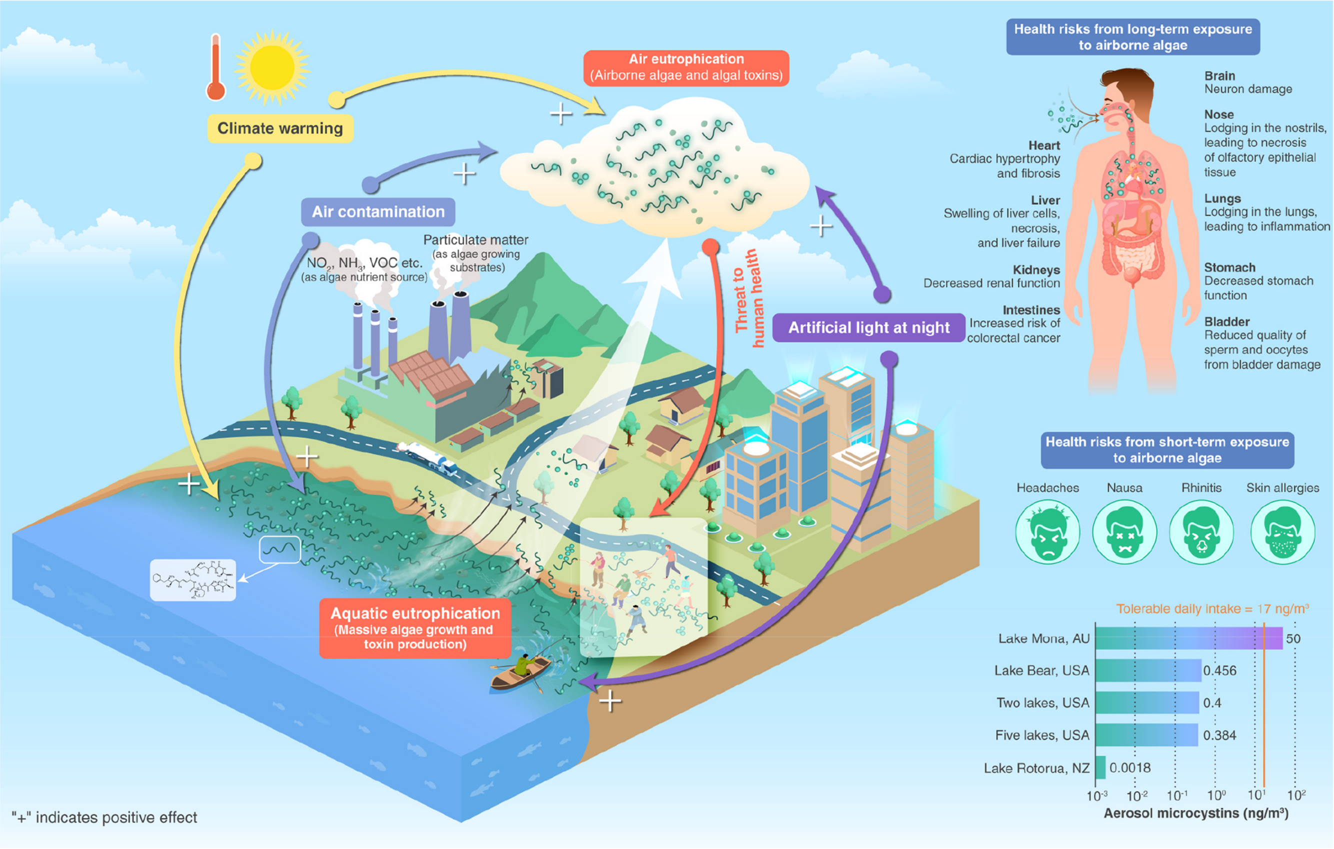

Figure 1. Development of "air eutrophication" and the potential impacts on human health and the maximum concentrations of microcystins measured in aerosols surrounding lakes. Aquatic eutrophication along with excessive nutrient loading promotes massive growth of algae, some of which are toxin-producing cyanobacteria. Aquatic algae can be emitted to the atmosphere where they form airborne assemblages. Air eutrophication develops along with the aquatic eutrophication and thereby provides algae sources, air contamination provides nutrients for airborne algae, and climate warming and artificial light at night stimulate the growth. Airborne algae and cyanotoxins can enter the body through human respiration, posing a potential threat to human health. Maximum concentrations of microcystins measured in aerosols surrounding lakes (see Chart 2 for the derivation of TDI—tolerable daily intake; see refs 25 and 73–77 for the source of measured aerosol microcystins).

the mass death of African elephants in Botswana in 2020, which was attributed to an amplified effect of eutrophication and harmful cyanobacterial blooms,[13] and the death of bald eagles (*Haliaeetus leucocephalus*) in Lake DeGray, Arkansas, after feeding on fish and waterfowl containing cyanotoxins cascading from cyanobacteria through the food chain.[14]

■ AIRBORNE ALGAE, ALGAL TOXINS, AND THE RISK OF IMPACTS ON PUBLIC HEALTH

Algae can be emitted from aquatic ecosystems into the atmosphere by wind-driven or ecosystem disturbances linked to animal movement and human activity[15−17] (Figure 1). Once emitted, the algae will be further dragged into the atmosphere by airborne turbulent kinetic energy,[18] even into the troposphere.[19] Recent studies have shown that 10% of microbes, including algae (0.5−5 μm in size) emitted from the sea, remain in the air 4 days after emission and that they can travel up to 11 000 km.[20] Airborne algae have also been detected in indoor environments.[21] Inhalation of these small-sized airborne algae is potentially harmful to animals and humans as they are deposited in the respiratory tract.[22] A high occurrence frequency of algae was observed in the upper respiratory tract in 92% of 77 study individuals who received a nasal swab and in the central airways in 79% of 29 individuals inspected with bronchoscopy,

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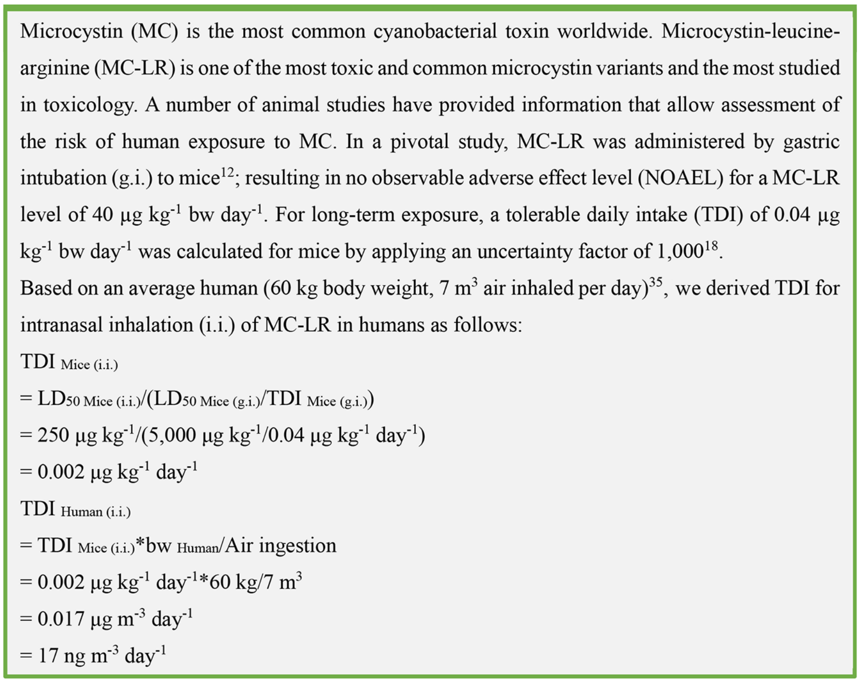
Table 1. Collected Studies on Cyanotoxin Concentrations in Aerosols[a]

cyanotoxin	aquatic microcystin (μg/L)	airborne microcystin (ng/m^3)	quantification method	aerosol collection method	source of water studied	study location	reference
microcystin	50	0.2	ELISA	personal sampler	laboratory	laboratory	74
microcystin	2.125	0.05	ELISA	high-volume sampler	field	Lake Bear, Michigan	74, 75
	2.625	0.023					
	3	0.057					
microcystin	82.275	0.0052	ELISA	high-volume sampler	field	Bloom Lake 1, California	76
	82.275	0.4		personal sampler		Bloom Lake 2, California	
	142.75	0.1					
	67.525	0.2					
microcystin	230	50	LC-MS/MS	lake spray aerosol generator	field (Lake Mona, AU)	laboratory	25
microcystin	155.987	0.0003	ELISA	high-volume sampler	field	Lake Rotorua, South Island, NZ	77
	1548.529	0.0018					
	447.839	0.0009					
nodularin	4.718	0.0073				Lake Forsyth, South Island, NZ	
	0.952	0.00023					
anatoxin-a	21	0.16	LC-MS/MS	air sampling device	field	Capaum Pond, Massachusetts	78

[a] Note: Data are average values.

Chart 2. TDI of MC-LR for Humans



Microcystin (MC) is the most common cyanobacterial toxin worldwide. Microcystin-leucine-arginine (MC-LR) is one of the most toxic and common microcystin variants and the most studied in toxicology. A number of animal studies have provided information that allow assessment of the risk of human exposure to MC. In a pivotal study, MC-LR was administered by gastric intubation (g.i.) to mice[12]; resulting in no observable adverse effect level (NOAEL) for a MC-LR level of 40 μg kg^{-1} bw day^{-1}. For long-term exposure, a tolerable daily intake (TDI) of 0.04 μg kg^{-1} bw day^{-1} was calculated for mice by applying an uncertainty factor of 1,000[18].

Based on an average human (60 kg body weight, 7 m^3 air inhaled per day)[35], we derived TDI for intranasal inhalation (i.i.) of MC-LR in humans as follows:

$\mathrm{TDI}_{\text{Mice (i.i.)}}$

$= \mathrm{LD}_{50\ \text{Mice (i.i.)}}/(\mathrm{LD}_{50\ \text{Mice (g.i.)}}/\mathrm{TDI}_{\text{Mice (g.i.)}})$

$= 250\ \mu\text{g kg}^{-1}/(5{,}000\ \mu\text{g kg}^{-1}/0.04\ \mu\text{g kg}^{-1}\ \text{day}^{-1})$

$= 0.002\ \mu\text{g kg}^{-1}\ \text{day}^{-1}$

$\mathrm{TDI}_{\text{Human (i.i.)}}$

$= \mathrm{TDI}_{\text{Mice (i.i.)}} * \mathrm{bw}_{\text{Human}}/\text{Air ingestion}$

$= 0.002\ \mu\text{g kg}^{-1}\ \text{day}^{-1} * 60\ \text{kg}/7\ \text{m}^3$

$= 0.017\ \mu\text{g m}^{-3}\ \text{day}^{-1}$

$= 17\ \text{ng m}^{-3}\ \text{day}^{-1}$

suggesting that airborne algae can be lodged in the nostrils and lungs after inhalation.[23]

Phytoplankton-generated aquatic toxins can be transferred to the air through aerosolization.[17] In addition, algal toxins produced by certain airborne algae constitute an important threat to human health.[24] In situ measurements in some lakes suggested a range of cyanotoxins between 0.00023 and 50 ng m^{-3} in aerosols (Figure 1, Table 1). When spraying lake water containing 230 μg L^{-1} MC into the air in the lab, MC in aerosol samples reached a level as high as 50 ng m^{-3}.[25] When female larval fruit flies (*Drosophila melanogaster*) were exposed to aerosolized cyanobacteria blooms, reduced lifespan and significant signs of cerebral degeneration were observed.[26] In mice where MC-LR was administered by inhalation or intratracheally, necrosis of the respiratory epithelium, bleeding in the liver, and damage to kidneys and intestines were observed.[27,28] For humans, inhalation of airborne algae and algal toxins may cause skin irritation, allergies, rhinitis, and respiratory problems[29] (Figure 1).

Despite their aquatic origin, most cyanotoxins tended to be more hazardous to terrestrial mammals (the median lethal dose of MC-LR by the intraperitoneal route was i.p. LD$_{50}$ = 50 μg kg^{-1} for tested mice) than to aquatic biota (i.p. LD$_{50}$ = 270−790 μg kg^{-1} for the tested fish *Hypophthalmichthys molitrix* and *Oreochromnis niloticus*).[30] Furthermore, toxin inhalation might be more dangerous than oral intake as suggested by the observed median lethal dose of 250 μg kg^{-1} MC-LR through intratracheal administration to mice compared to 3000 μg kg^{-1} MC-LR through oral administration.[25,31] Inhalation of MC-LR in mice was found to induce necrosis of the respiratory epithelium,

Chart 3. Research Agenda

To study the development of “air eutrophication” and the impacts of airborne algae and toxins, we need multifaceted and multidisciplinary approaches, including:

I. Well-defined common protocols providing guides to collect and measure airborne algae and toxins and to study the toxicity of airborne algae exposure.

II. Scanning the size spectrum of airborne algae and exploring the role of particle size in the development of “air eutrophication”.

III. High frequency monitoring to quantify the algae exchange at the water-air interface and the quantitative link of algae and toxin concentrations between water and air.

IV. Modeling the key hydrological, meteorological, and atmospheric processes influencing the formation and transport of airborne algae at lake and cross-lake scales.

V. Controlled experiments to reveal the potential growth of airborne algae and toxin production under varying atmospheric conditions, including nutrient concentration, light intensity and quality, and air temperature and moisture.

VI. Epidemiological research to explore the potential contribution of “air eutrophication” to affecting human health, particularly of those working on harvesting blooming cyanobacteria.

which further promoted the absorption of the toxin into the bloodstream.[27] Inhalation directly impacts the respiratory system, and inhaled toxins can directly enter the organs. In addition, studies on the immunological effects of vaccines by different routes of administration have revealed that inhaled aerosol vaccines provide better protection and stimulate stronger immune responses than nasal spray vaccines.[32] The inhaled aerosol passes through the nasal passage and delivers the vaccine droplets deep into the airways, inducing a broad protective immune response.[33] This also reinforces the view that nasal inhalation of aerosolized algae and algal toxins may have more potent toxic effects. To test this, we calculated a tolerable daily intake (TDI) of $17\ \mathrm{ng\ m^{-3}\ day^{-1}}$ for the nasal intake of MC-LR in humans, based on the TDI in mice[18] and the average human body weight (60 kg body weight, $7\ \mathrm{m^3}$ of air inhaled per day)[34] (see Chart 2 for the derivation of TDI).

MULTIPLE DRIVERS POTENTIALLY ACCELERATING AIR EUTROPHICATION

There is growing evidence that algal blooms in eutrophic aquatic ecosystems have increased in diversity, frequency, size, and geographical extent in recent decades,[35] implying an enriched source of airborne algae.[36,37] Climate warming, with the additional light hours and richer light intensities provided by artificial light at night (ALAN), may directly favor the formation, transportation, and development of airborne algae and increase the potential of toxin production and hence the risk of human exposure to toxins. In the future, humans and wildlife are expected to face an increasing risk of exposure to airborne algae and the cyanotoxins that they produce in cyanobacteria-impacted aquatic ecosystems.

It is widely recognized that eutrophication is accelerating in response to global warming, particularly in recent years.[38,39] Widespread, prolonged, and unprecedented extreme heat has occurred in 2022 in the Northern Hemisphere, exceeding the expectations of many climate scientists.[40] The preliminary results of a study of airborne algae conducted in the southern coastal zone of the Baltic Sea from January to December 2022 suggest that the total amount of airborne cyanobacteria was positively correlated with the concentration of MC-LR, and the increase of airborne cyanobacteria and airborne algae was mainly related to the rise in temperatures.[41] The proportion of toxic species or strains and the release of toxins tend to increase in a hotter climate,[42,43] potentially enhancing the risk of airborne algal toxin production. Climate warming may also favor the growth and competition of small-sized freshwater and marine algae species,[44,45] which are more likely to be emitted into the atmosphere and carried to distant locations away from their sources than large-sized species.[46]

Light availability is another key factor controlling the growth of algae in aquatic ecosystems.[47] Urbanization has led to rapid expansion of ALAN in space at a rate of 2−6% per year.[48−50] With the advent of a wide range of lighting devices, both cool and warm white ALAN has become increasingly abundant.[51,52] For freshwater cyanobacteria, warmer white ALAN means a higher photosystem II:photosystem I ratio and hence stronger photosynthesis activities.[53] A positive correlation was observed between photosynthetically active radiation and toxin production in *Microcystis aeruginosa*.[54] The proportion of cyanobacteria was found to increase by 17%, while the proportion of diatoms and chrysophytes decreased in spring when exposed to ALAN.[55] A study conducted in the southern Baltic Sea region from 2018 to 2020 showed a positive effect of increased light intensity on the growth of the cyanobacterium *Nostoc* sp. and the diatoms *Nitzschia* sp., *Amphora* sp., and *Halamphora* sp.[56] Therefore, the expansion of ALAN may have a positive effect on the development of “air eutrophication” through enhancing the growth of airborne algae: stimulating the growth of some algae and the production of algal toxins in the aquatic ecosystem, hence providing a richer source of algal and toxin emissions to the atmosphere.

Atmospheric deposition of pollutants has received attention as an important nutrient source for phytoplankton in aquatic ecosystems.[57] The contribution of airborne particles is high and increasing in various nutrients such as nitrogen, phosphorus, and carbonaceous compounds.[58−60] A global increase of 12.8 ± 1.3% of atmospheric ammonia (NH_3) was recorded between 2008 and 2018.[61] Significant increases in nitrogen dioxide (NO_2) and reactive volatile organic compounds have also been widely reported, particularly in tropical cities.[62] It has been shown that nitrogen-enriched acid rain and anthropogenic atmospheric nitrogen deposition can enhance marine primary production.[63,64] For example, it was found that atmospheric dry deposition of nutrients along the coastal Bay of Bengal resulted in an increase in primary production from 3% to 19%.[65] Aerosol deposits from wildfires, metals carried by volcanic lava, and deposition of nitrogen and phosphorus from burning fossil fuels have also been reported to stimulate the growth of aquatic phytoplankton.[66,67] But what about the stimulation of the growth of airborne algae? A strong positive correlation was found between aerosol bacterial gene abundance and air pollutant concentrations and the air quality index in a study on the atmosphere of Hefei City, China.[68] Whether a similar direct stimulating effect on the development of airborne algae and toxins occurs with increasing nutrient pollution in the air is an open question but important to elucidate given the potential health problems associated with some algae and their toxins in regions with high production of such algae in the water.

In contrast to the widely reported fundamental role of nutrients in the growth of aquatic algae, few studies are available on airborne algae, unfortunately.

■ URGENT NEED FOR RESEARCH INTO AIR EUTROPHICATION AND DEVELOPMENT OF SOLUTIONS

Currently, little research has been carried out on airborne algae, their prevalence, and impacts. However, we cannot wait for consensus based on ample evidence when it comes to potentially major threats to public health. Atmospheric bacteria and fungi are an important component of bioaerosols, and their community composition is influenced by a complex set of environmental factors.[69] At the same time, they are more abundant than airborne algae and can pose a serious threat to human health and the environment as pathogens and allergens.[70,71] As such, atmospheric bacteria and fungi will also play a non-negligible role in promoting air eutrophication. Therefore, we consider "air eutrophication" as a potentially important research field requiring a cross-discipline research effort, including medical, physical, hydrological, geological, and ecological expertise (Chart 3). This research agenda is timely for applying the precautionary principle as a critical risk management strategy for ensuring the safety of public health and the environment worldwide, particularly in the areas with extremely high risk of cyanotoxin exposure and climate changes.[72]

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Author Contributions

Y.F.S., Y.G., and H.W. conceptualized and designed the study. Y.F.S. and H.W. visualized the tables and figures and wrote the original draft manuscript. Y.G., C.X., Y.L., X.Z., Q.L., E.J., H.W., and P.X. reviewed and edited the manuscript. All authors revised the manuscript, approved the final manuscript, and agreed to take responsibility for all aspects of the work.

Notes

The authors declare no competing financial interest.

Biographies

Prof. Dr. Haijun Wang has been working on aquatic eutrophication and cyanobacteria bloom for 22 years. Before moving to Yunnan University with a Grant of High-level Talented Scientist, he had been working for 20 years at the Institute of Hydrobiology, Chinese Academy of Sciences. He is now the deputy director of Institute for Ecological Research and Pollution Control of Plateau Lakes, School of Ecology and Environmental Sciences, Yunnan University. He was selected as an excellent member of the Youth Innovation Promotion Association of Chinese Academy of Sciences in 2018.

Prof. Dr. Ping Xie is a principal scientist at the Institute of Hydrobiology, Chinese Academy of Sciences, and is the director of Water Subcenter of Chinese Ecosystem Research Network (CERN) and vice director for the State Key Laboratory of Freshwater Ecology and Biotechnology, China, and the dean of Institute for Ecological Research and Pollution Control of Plateau Lakes, School of Ecology and Environmental Sciences, Yunnan University. He has very strong background in aquatic eutrophication, cyanobacteria blooms, and ecological impacts of cyanobacteria and cyanotoxins. Prof. Xie received his Ph.D. from University of Tsukuba, Japan, in 1989. He won an international award, Biwako Prize for Ecology, in 1999. He has published more than 250 SCI-indexed papers as the first or corresponding author. His articles have been cited over 10 000 times with an H index of 50. From 2014 to 2021, he has been on the list of highly cited Chinese scholars in Environmental Science or Biology released by Elsevier.

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