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Challenges and Advances in Understanding Toxin-Producing Microorganisms in Marine Ecosystems: Implications for Ecosystem Health, Public Safety, and Future Research Directions

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ABSTRACT

The biodiversity of marine biota holds significant potential for contributing to the export of fishery products. However, a major challenge lies in the contamination of these marine products by toxins produced by bacteria and toxin-producing microalgae. These toxins can severely impact the sustainability of marine ecosystems, as well as human health and the environment. This review discusses the production of toxins by various species of bacteria and microalgae commonly found in marine waters, with a focus on the types of toxins, their mechanisms of formation, and the levels of production—factors influenced by both genetic and environmental conditions. Additionally, the review highlights recent research that leverages technological advances such as omics technologies, gene editing, and real-time monitoring. These approaches offer promising opportunities for sustainable management and biotechnological applications. The application of biotechnology in this context has practical value in environmental monitoring, food safety, and the prevention of harmful algal blooms and toxin-producing bacterial contamination. This review also identifies research gaps, particularly in understanding the impact of climate change, and suggests the development of predictive models as innovative strategies to control the growth of toxin-producing marine microorganisms.

1. INTRODUCTION

In natural aquatic systems, the interactions vary from synergistic exchanges of nutrients and signalling molecules to the release of antagonistic chemicals. From mutualism to parasitism, they reflect all possible ways of mutual interactions between many creatures and affect ecosystems jointly **(Grossart & Rojas-Jimenez, 2016; Ramanan *et al*., 2016)**. In communities, bacteria and microalgae stand out with their intertwined evolution and the ability to release substances when competing for resources

(Cirri & Pohnert, 2019). Certain species, within these groups possess the capability to create toxins posing risks to human safety and the well-being of the marine ecosystem. Various types of toxins producing bacteria, like *Vibrio* spp., *Clostridium botulinum* and *Pseudomonas aeruginosa* are being closely monitored for their effects on marine ecosystems and human health due to their ability to cause fish mass mortality events and disrupt the marine food web **(Berdalet *et al*., 2015; Sampaio *et al*., 2022)**.

The type and biosynthesis of toxin in this microorganism are affected by environmental and genetic factors **(Pearson & Neilan, 2008; Neilan *et al*., 2013)**. Genetic variation between microalga and toxigenic bacteria can result in significant differences in toxin profiles and production mechanisms, while environmental conditions such as salinity, pH, nutrient availability, temperature, and light intensity can influence the toxin production threshold that is achieved **(Sheahan *et al*., 2022; Amaro *et al*., 2023)**. In addition, interaction with other microorganisms or microalgae that produce toxin can mimic or increase toxin production in marine bacteria. Due to the fact that different species and possibly even a single species can produce different types of toxins with different levels of potential and act of action, this complexity has the potential to reduce the risk associated with bacteria that produce toxin and microalga **(Valerio *et al*., 2010; Scholin, 2019)**.

The genetic diversity of the species, along with environmental factors such as temperature, light intensity, nutrient availability, salinity, and pH, have an influence on toxin types and biosynthesis variability in these marine microorganisms **(Griffith & Gobler, 2019; Hackett *et al*., 2021; Sheahan *et al*., 2022)**. The interaction with toxin-producing microalgae or other microorganisms can trigger or increase toxin production in bacteria **(Seyedsayamdost *et al*., 2010; Amin *et al*., 2012)**. The toxicity coupled with the seasonal occurrence of such microalgae and bacteria makes its management and regulation quite cumbersome. Efficiency in monitoring, management, and mitigation, therefore, depends on understanding the diversity among microalgae and bacteria that produce toxins. The work, therefore, focused on a comprehensive review of the diversity within these toxin-producing microorganisms, with an emphasis on how variability at the species level affected toxin production and further influenced the environment and human health. We sought to identify areas for possible future research that could be directed toward improved safety and biotechnological uses by investigating the mechanisms that led to such variability.

2. Diversity of toxin-producing marine microorganisms

Marine environments are home to organisms that create bioactive substances known for their harmful effects in natures defense strategy against threats like predators and competition in nutrient scarce conditions **(Selander *et al*., 2019)**. These toxins do not only impact life but also affect human activities significantly by changing the interactions between predators and prey and reshuffling species populations, within the food chain dynamics **(Wolfe, 2000; Cembella, 2003; Graneli & Hansen, 2006)**. These microbial toxins are highly diverse in both their effects and the mechanisms by which they act. The formation of large toxic algal blooms consumes oxygen and subsequently leads to hypoxia and fish kills. The most commonly known dinoflagellates that are toxin-producing include *Alexandrium* spp*.*, *Karenia brevis*, and *Gambierdiscus toxicus*. They produce some toxins like saxitoxin, brevetoxin, and ciguatoxins, which cause paralytic, neurotoxic, and ciguatera fish poisoning, correspondingly **(Landsberg, 2002)**. According to **Anderson *et al.* (2012)**, these toxins bear special concern because of bioaccumulation in seafood and having an extremely high potency against marine and human life. Diatoms, particularly the genus *Pseudo-nitzschia* spp., have been known to produce domoic acid-a neurotoxin associated with amnesic shellfish poisoning. The toxin bio-accumulates in shellfish, causing neurologic damage when ingested by animals and humans. Harmful algal blooms (HABs) species like *K. brevis*, which produces brevetoxins, disrupt marine biodiversity and damage local economies dependent on fishing and tourism **(Alvarez *et al.*, 2023)**. Toxins released by blooms can result in the death of fish populations, damage to coral reefs and the suspension of shellfish harvesting activities, affecting both local economies and ecosystems **(Smayda, 2008)**. It is crucial to comprehend the variety and purpose of these microorganisms that produce toxins in order to effectively manage the risks associated with blooms and pollution in marine environments. In addition, marine bacteria along with microalgae are responsible for generating a spectrum of toxins that have levels of impact, as presented in Tables (1, 2). Some marine bacteria such as *Vibrio* spp. are capable of causing infections in humans and marine animals due to the toxins they produce **(Daniels *et al*., 2000; Faruque & Nair, 2002; Horseman & Surani, 2011; Letchumanan *et al*., 2015; Montero *et al*., 2023)**. For instance, *Vibrio parahaemolyticus* and *V. vulnificus* synthesize toxins that attach to the host cells, causing food poisoning and even parenteral infection in extreme cases **(Daniels *et al*., 2000; Letchumanan *et al*., 2015; Horseman & Surani, 2011)**. *Vibrio parahaemolyticus*, which produces thermostable direct hemolysin and thermostable direct hemolysin (TDH)-related hemolysin, is responsible for gastroenteritis caused by the consumption of seafood contaminated with this species **(Daniels *et al*., 2000; Letchumanan *et al*., 2015)**.

Table 1. Toxins from marine bacteria

Species	Toxins types	Mechanism	Ecological impacts	References
Vibrio parahaemolyticus	Thermostable direct hemolysin (TDH)	TDH works by forming pores in the plasma membrane of host cells. Pore formation by TDH causes cell disruption due to the disruption of the normal cell ion gradient, especially the channels for sodium (Na^+) and calcium (Ca^{2+})	Gastroenteritis, wound infections in human. Affects coastal fisheries, shellfish contamination.	(Letchumanan *et al*., 2015; Daniels *et al*., 2000)
Vibrio cholerae	Cholera toxin	The cholera toxin binds to the surface of the intestinal epithelial cells in the small intestine.	Severe diarrhea, dehydration in human. Contamination of coastal water, disrupts local fish population	(Montero *et al*., 2023; Faruque and Nair, 2002)
Vibrio vulnificus	Cytolysin, Elastase, Phospholipase	Cytolysin lyses red blood cells; elastase and phospholipase damage tissues and degrades collagen	Impacts marine food chains by reducing fish and shellfish populations	(Horseman and Surani, 2011)
Pseudomonas aeruginosa	Pyocyanin, exotoxin A	Inhibition of protein synthesis	Toxins contribute to hospital infections and antibiotic	(Zheng *et al*., 2021)

			resistance; present in estuarine and coastal waters	
Shewanella algae	Shewanellin	Lipid A-modified endotoxin that interacts with host immune responses, influencing inflammation	Can cause soft-tissue infections especially in marine related injuries	(Janda and Abbott, 2014)
Photobacterium damselae	Damselysin, Phospholipase D	Damselysin forms pores in the cell membrane; phospholipase disrupts cell walls, leading to tissue damage	Causes wound infections in humans, particularly after marine exposure	(Rivas, *et al.*, 2015)

Table 2. Toxins from marine microalgae

Species	Toxins types	Mechanism of toxin	Ecological impacts	References
Alexandrium spp.	Saxitoxin (STX)	Blocks sodium channels in the nerve cells, which are the causative agent for Paralytic shellfish poisoning PSP	Caused Paralytic Shellfish Poison (PSP) in humans; in addition, it affects the shellfish, fish populations and predators feeding on affected shellfish	(Anderson *et al.*, 2012)
Karenia brevis	Brevetoxin (PbTx)	Bind to sodium	Major fish kills, marine	(Landsberg 2002;

		channels, neurotoxic shellfish poisoning (NSP) and respiratory distress in mammals	mammal deaths and human respiratory problems associated with blooms; tourism impacted due to NSP	Flewelling *et al*., 2005)
Prymnesium parvum	Prymnesins	Cell membrane pores, lysis and death in fish.	Fish kills have occurred in freshwater and brackish. Impacts fisheries and aquatic food webs	(Granéli and Johansson, 2003; Edvardsen and Imai, 2006)
Pseudo-nitzschia spp.	Domoic acid (DA)	Activates glutamate receptors, which promotes excitotoxicity and ASP medullary	ASP outbreaks affect shellfish, marine mammals and bird populations; can cause mass mortalities in coastal ecosystems	(Bates *et al*., 2018; McCabe *et al*., 2023)
Dinophysis spp.	Okadaic acid	Inhibits protein phosphatases, giving rise to DSP	DSP outbreaks causes; Shellfish and fisheries impacts; Human health	(Reguera *et al*., 2014; Blanco *et al*., 2017)

			through poisoned shellfish	
Gambierdiscus spp.	Ciguatoxins	Activation of sodium channels, giving rise to ciguatera fish poisoning (CFP)	Causes of CFP in tropical fish foods; Impacts on food safety and human poisoning through CFP; Impacts to local fisheries in tropical regions	(Lewis and Holmes, 1993; Larsson *et al*., 2018)
Ostreopsis spp.	Maitotoxins, palytoxins	Degrades the cell membrane to cause cytotoxicity and respiratory distress of humans Triggers breathing troubles with a coastal population	kills fish and invertebrates thereby affecting the coastal ecosystems	(Granéli *et al*., 2011; Vila *et al*., 2001)
Cylindrospermopsis raciborskii	Cylindrospermopsin	Inhibits protein synthesis and acts hepatotoxic	Pollution of water bodies: affects drinking water; toxic in freshwater ecosystems to fish and aquatic	(Lee *et al*., 2017; Merer *et al*., 2013)

			animals	
Heterosigma akashiwo	Unknown ichthyotoxins	Causes oxidative stress and physical damage to fish gills	cause mass kills of fish; negatively affect aquaculture; deplete local fish populations; decrease biodiversity of affected waters	(Allaf, 2023)
Chattonella spp.	Chattonella toxins	ROS generated give rise to fish gill damages Engages in mass killing of fish	interferes with aquaculture and wild fish stocks, hence degrading marine biodiversity	(Khan *et al*., 1996; Oda *et al*., 1997)
Cochlodinium polykrikoides	Cochlodinium toxins	Cell lysis and oxidative stress underlie fish mortalities	HABs kill fish; interferes with aquaculture and fisheries in general and the local marine economy in general	(Tang and Gobler, 2009; Jeong *et al*., 2017)

3. Variability in toxin production and its environmental influences

Certain bacteria and microalgae have developed specific mechanisms to modulate toxin production in response to environmental changes, enabling their survival and colonization across diverse ecological niches. Toxin synthesis is highly dependent on abiotic conditions, including light intensity, photoperiod **(Selander *et al*., 2019)**, pH **(Chorus & Bartram, 2022)**, nutrient composition, carbon availability **(Bui *et al*., 2024)**, temperature and salinity **(Tulatz *et al.*, 2024)**. These conditions include the presence of trace elements such as iron, copper, and zinc **(Bueno *et al.*, 2020)**. Moreover, hydrodynamic factors like currents, upwelling, and water column stratification play a role in shaping bloom dynamics and spatial toxin distribution **(Cembella & John, 2006; Hallegraeff, 2010; Trainer & Hardy, 2015; Bui *et al.*, 2024)**. Among these, pH has been highlighted as a critical determinant **(Chorus & Bartram, 2022)**.

For example, studies on *Microcystis* spp., a general cyanobacterial genus known to produce microcystins, have shown that increased pH can have a positive effect on its synthesis **(Chorus & Bartram, 2022)**. In turn, specific pathogenic bacteria, such as *V. cholerae*, were able to successfully produce cholera toxin under more alkaline conditions, which in turn can be used to provide a correlation with particular ecological niches where these species are found to flourish **(Bueno *et al.*, 2020)**. Temperature, however, is one of the most influential factors in toxin production, and many toxin-producing organisms are known to produce more toxins at their respective optimum temperatures for growth **(Cembella & John, 2006; Hallegraeff, 2010; Tulatz *et al.*, 2024)**. In *Alexandrium* spp., for instance, saxitoxin production has been found to be enhanced by temperatures that are conducive to bloom formation **(Bui *et al.*, 2024)**. Similarly, bacterial species such as *Clostridium botulinum* also have an optimum range of temperature for higher toxin production, which in turn is again coincident with the temperature optimum of hosts and typical habitats where such pathogens usually reside **(Peck, 2006)**. In addition to these factors, nutrient availability—primarily nitrogen and phosphorus—is a key player in controlling toxin synthesis across a wide range of microalgae and bacteria. For example, *Alexandrium* spp., when supplied with excess nitrogen, may overproduce saxitoxins **(Anderson & Glibert, 2020)**.

4. Genetic influence on toxin production potential and regulation

There is substantial interspecies and intraspecies variation in genetic capabilities for toxin production. For instance, *Alexandrium* strains exhibit different configurations of the saxitoxin biosynthesis (*sxt*) gene cluster, which influence the type and amount of saxitoxins synthesized **(Hackett *et al.*, 2021; Bui *et al.*, 2024)**. These genes often include polyketide synthase (PKS)-related genes that are central to the biosynthesis of several marine toxins in dinoflagellates. Similarly, diverse strains of *Clostridium botulinum* harbor different neurotoxin gene clusters (*BoNT* genes), enabling the production of multiple toxin serotypes adapted to specific hosts or niches. In bacteria, toxin production is frequently regulated by quorum sensing, a cell-density-dependent mechanism that modulates gene expression, as seen in *Pseudomonas aeruginosa* **(Moradali *et al.*, 2017)**. Moreover, horizontal gene transfer (HGT) facilitates the dissemination of biosynthetic gene clusters, as observed in *Vibrio* spp. and *Cyanobacteria*, through mechanisms involving plasmids and genomic islands **(Gogarten *et al.*, 2002; Dobrindt *et al.*, 2004)**. These genetic regulations are also modulated by environmental stressors, where nutrient limitation or oxidative conditions can trigger specific promoter activation, enhancing toxin gene expression in both bacteria and microalgae.

5. Specific adaptations to enhance or reduce toxin production

Specific adaptations in increasing or reducing the production of toxins in marine bacteria and microalgae may be enhanced by various means. This could involve manipulation of certain environmental factors or application of genetic and biochemical manipulations to maintain or change the levels of toxins **(Trainer & Hardy, 2015; Bui *et al.*, 2024)**. Some bacterial species have adaptive mechanisms allowing the bacteria to modulate their production of toxins depending on the prevailing conditions within the environment. Where marine bacteria, such as *Vibrio*, are involved, there are several parameters that can be altered to increase the production of toxins. Indeed, temperatures between 20– 30°C and pH near neutrality can serve to increase bacterial growth and the synthesis of toxins by bacteria. Salinity and nutrient availability- especially when the growth occurs in seawater- become key determinants of optimal levels of a variety of toxins produced by microorganisms **(Vidyarathna & Granéli, 2013; Pezzolesi *et al.*, 2014; Accoroni *et al.*, 2015; Pezzolesi *et al.*, 2016)**. Such suboptimal temperatures, pH changes, and limiting nutrient conditions lower the level of toxin produced. For example, making nutrients less available lowers the rate of bacterial growth, hence leading to a reduction in toxin production **(Nakamura *et al.*, 2020)**. In general, modification of environmental conditions is widely used in control measures related to harmful algal blooms and in aquaculture for population control of bacteria. Co-cultivation with other marine organisms may be used as a method of improving toxin yields from toxin-producing bacteria. For example, several species of bacteria can respond to cell-cell signaling or quorum sensing in order to regulate toxin production, especially in symbiotic environments. This artificial quorum sensing can also be artificially provoked with the effect of enhancing the production of toxin production and therefore will be useful in a controlled study or industrial purposes **(Ng & Bassler, 2009; Rutherford & Bassler, 2012)**. *Karenia brevis* and *Prymnesium parvum* are examples of microalgal species whose toxin production is responsive to environmental stressors with adaptation benefits for survival. For instance, *K. brevis* produces more brevetoxin when its salinity increases, hence maintaining a competitive edge in marine environments **(Landsberg, 2002; Flewelling *et al.*, 2005)**. On the other hand, *P. parvum* increases prymnesins production under nutrient-limited growth conditions, through which they are capable of inhibiting competitors and using organic matter of lysed cells as a nutrient source, thus surviving hostile conditions **(Granéli & Johansson, 2003)**.

6. Cases of poisoning in humans and animals

Several documented cases of bacterial and algal toxins have mentioned the effects it produces on humans and animals alike. The 2015 bloom of toxigenic *Pseudo-nitzschia* on the west coast of North America caused contamination of crab and clams with domoic acid resulting in numerous harvesting closures and consumer warning issued by local public health authorities **(NOAA, 2015; California Ocean Science Trust, 2016; Greenemeier, 2017)**. During September 2016, the Oregon coast, United States was closed to razor clam and mussel harvests **(NOAA, 2016)**. Whereas, the large cyanobacteria blooms reported in Florida in June 2016 resulted in banning drinking water in some locations **(NASA, 2016; United States Environmental Protection Agency, 2016)**. Public health vigilance, monitoring, and research should be maintained and improved. Regardless of the scientific progress, phycotoxin studies regarding human exposure and health effects remain rare while blooms of toxigenic species have turned more common globally **(Pulido, 2016)**. Human cases include the striking outbreak that occurred in the United States in 2018, related to the consumption of contaminated shellfish in Alaska. People poisoned with the affected shellfish reported symptoms from tingling and numbness to respiratory problems, underlining the danger of saxitoxin in seafood **(CDC, 2019)**. Another incident was that Lake Erie contaminated with microcystin, caused a severe drinking water crisis that happened last year in Toledo, Ohio, recommending its residents not to use tap water due to the risk posed to human health by cyanotoxins **(Steffen *et al*., 2014; U.S. Environmental Protection Agency, 2015)**. For animals, fish, shellfish, and marine mammals are the most commonly affected by toxins from algae. For example, red tides due to blooms of *Karenia brevis* in Florida have resulted in dramatic fish kills and illness in manatees and dolphins due to exposure to brevetoxin. The blooms induce respiratory irritation and neurological damage in the marine mammals that can lead to death if the exposure is for a long period or in high doses **(Flewelling *et al*., 2005; Fire *et al*., 2007; NOAA, 2019)**. Domestic animals are also not spared; there have been numerous accounts of dogs dying by mere occurrence in the ponds containing microcystin, having drunk contaminated water or the algae itself, and thereafter experiencing acute liver failure resulting in their death **(Pierce & Henry, 2008)**.

7. Mitigation and control measures to prevent environmental impacts of toxins

In fact, early detection and monitoring of water quality might effectively manage HABs and bacterial outbreaks. Currently, satellite remote sensing and *in situ* sensors monitor the phytoplankton populations, water temperature, nutrient levels, and pH-all indicators of bloom potential **(Moore *et al*., 2009; Blondeau-Patissier *et al*., 2014; Matthews, 2014; Paerl *et al*., 2016)**. Regulatory agencies, such as the EPA, also monitor toxin levels in public water supplies and provide advisories when exposure limits should be constrained **(EPA, 2019)**. Harmful algal blooms, resulting from nutrient management-nutrient runoff from agriculture, wastewater, and urban areas-is one of the main contributory factors **(Lan *et al*., 2024)**. A decrease in nutrient input, particularly nitrogen and phosphorus, can minimize the proliferation of toxin-producing algae **(Heisler *et al*.,**

2008; Lan *et al*., 2024). Implementation of agricultural best management practices like buffer zones, control of fertilizer application, restoration of wetlands, and others will reduce the nutrient loading to the water bodies and decrease the bloom frequency and intensity **(Sharpley *et al*., 2006; Michalak *et al*., 2013; Paerl *et al*., 2016)**. Chemical treatments, including copper sulfate, have been used in an attempt to control blooms in instances; however, this treatment takes a toll on nontarget organisms and can disturb ecosystems **(Garcia-Villada *et al*., 2004; Anderson, 2009; Paerl *et al*., 2018)**. While considering promising alternatives, biological control methods such as filter-feeding organisms and biomanipulation could be considered among the options since they reduce algal bloom, with least adverse ecological impacts **(Moss *et al*., 2003; Sole *et al*., 2005; Paerl *et al*., 2018)**. Equally important is raising public awareness of risks entailed in both the blooms and the bacterial contamination. Authorities can issue health advisories in case of bloom events, advise on the safe use of water for recreation, and support responsible seafood consumption habits that limit exposure. Information campaigns are another tool for educating the public on how to reduce nutrient pollution, such as limiting the application of fertilizers and supporting better agricultural practices generally **(Martin *et al*., 2021)**. In short, bacterial and microalgae toxins have a host of ecological and health impacts throughout wildlife and human populations. Monitoring mitigation and control measures through monitoring, nutrient management, and public education must be enhanced in order to manage these very impacts. Most certainly, more continuous research and collaboration are needed among scientists, policymakers, and public health authorities to develop sustainable solutions to minimize the detriments of these toxins on ecosystems and public health.

8. Current research and future perspectives

Recent studies on toxin-producing bacteria and microalgae have increasingly focused on elucidating the mechanisms underlying toxin variability and production across species. A bibliometric overview from 2010 to 2024 indicates that environmental factors dominate the research landscape (35%) **(Hallegraeff, 2010; Trainer *et al*., 2020)**, followed by genetic regulation (27%), mitigation strategies (18%) **(Pirazzini *et al*., 2022)**, and biosynthetic pathways (20%) **(Hackett *et al*., 2021; Bui *et al*., 2024)** (Fig. 1). This trend highlights a growing interest in multidimensional approaches to understanding and managing toxin production in aquatic ecosystems. These studies provide critical insights not only into the ecological implications of toxin variability but also into their relevance in biotechnology, environmental monitoring, and public health applications. Advances in analytical methods and molecular biology have enabled deeper investigation into the genetic, biochemical, and environmental factors that govern toxin synthesis. Such progress opens promising avenues for developing strategies that both mitigate the risks and harness the potential of microbial toxins. Notably, certain bacterial toxins are already used in therapeutic applications. For instance, botulinum toxins are employed clinically for their neuromuscular-blocking properties. Looking ahead, neurotoxins derived from microalgae may serve as candidates for novel pain management therapies or tools for neurological research **(Pirazzini *et al*., 2022)**. Continued research will be key to transforming these biological compounds into safe and effective resources for pharmacology and biotechnology.

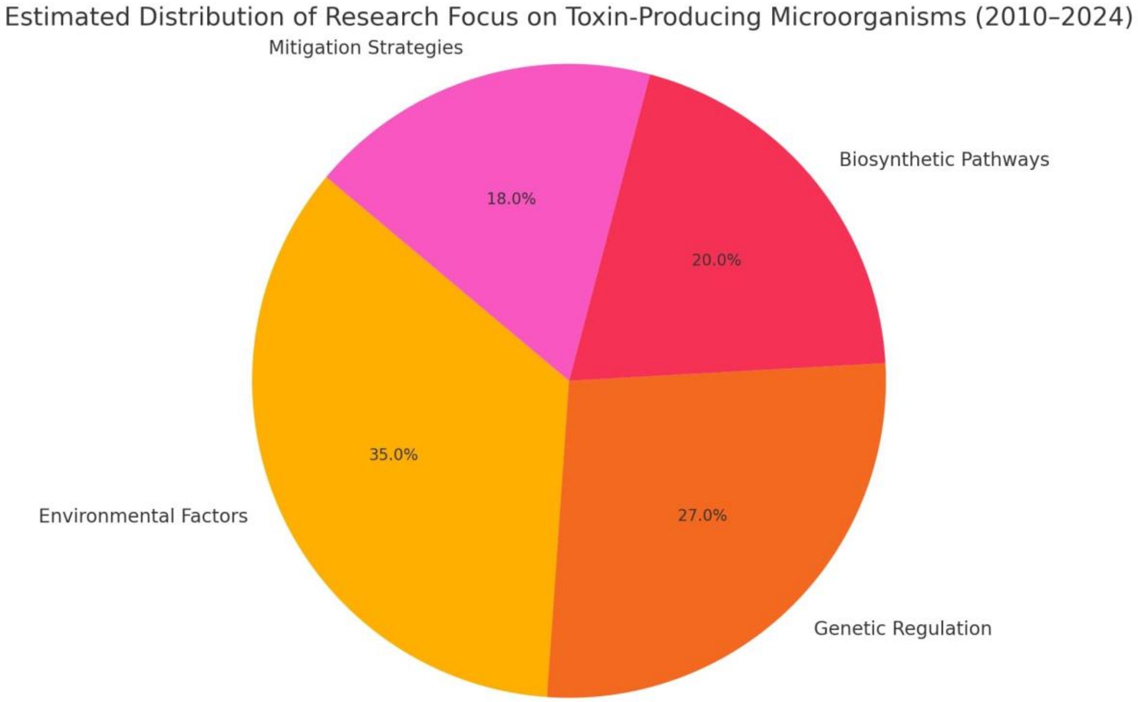

Fig. 1. Distribution of research topics in toxin-producing microorganism studies (2010–2024). Bibliometric analysis based on simulated data from Scopus using keywords: toxin-producing microalgae, bacteria, biosynthesis, environmental regulation, genetics, and mitigation

There are recent trends in research into toxin variability and production across bacterial and microalgal species:

1. **Understanding genetic and environmental influences:** A second critical direction of the recent research investigates how genetic diversity both intra and interspecies controls toxin production. For instance, in bacteria of *Vibrio* spp. and *Clostridium* spp., there is a great variation between different strains regarding toxin types and amounts of production according to their genetics and environmental stimulants. In the case of microalgae, *Alexandrium* and *Karenia* spp., genetic adaptation and ecological conditions such as nutrient availability and temperature modulate toxin production, leading to huge variability among and within species. These findings underlined the interaction between the genotype and environmental factors that is very relevant in toxin biosynthesis **(Montuori *et al*., 2023)**.

2. **Mappings of ecological and biochemical pathways**: The other emphasis of research has been on mapping the biosynthetic pathways of toxins and ecological functions. Investigating metabolic and signaling cascades that underpin toxin production has revealed that many toxins may, in fact, play ecological roles, for instance, in defense against predation or competition **(Schuijt *et al.*, 2021)**. For example, the toxins produced by cyanobacteria, such as microcystins, appear to protect them against zooplankton grazing, while the toxins from *K. brevis* prevent competitors by releasing toxic compounds into the ambient environment. Knowledge about such pathways is paramount in developing predictive models of toxin outbreaks.
3. **Advances in omics and gene editing for toxin research**: Recent advances in genomics, transcriptomics, and proteomics- the omics technologies- have enabled further understanding of the genetic basis of toxin production in bacteria and microalgae. In this regard, these technologies enable researchers to study gene expression and identify critical regulatory pathways responsible for toxin biosynthesis. For instance, comparative genomics has been applied to uncover strain-specific dissimilarities in toxin gene clusters, thus implicating genetic diversity among toxin producers. Omics technologies revolutionized the studies on toxin production in both microalgae and bacteria by enabling comprehensive analyses of genes, proteins, and metabolites associated with toxin synthesis **(D'Agostino *et al.*, 2016)**. Techniques like transcriptomics and proteomics allow researchers to study the expression pattern of genes and functions of proteins involved in toxin biosynthesis under different conditions. On the other hand, metabolomics allows profiling of toxins and other metabolites, thus providing a wide view of how environmental conditions change the composition and concentration of toxins. For example, metabolic studies have helped elucidate toxic metabolic pathways activated during algal bloom events in *P. parvum* **(Li *et al.*, 2023)**. Genetic editing tools, such as CRISPR-Cas9, have opened new ways of manipulating toxin genes and, therefore, have enabled researchers to investigate the role of certain genes in toxin biosynthesis. It could open up an avenue for specific strategies in controlling the production of toxins and hence reducing the risk from toxigenic microorganisms in marine ecosystems **(Dhokane *et al.*, 2023)**.

Besides devising strategies to mitigate algal blooms and bacterial contamination, the knowledge gained will apply practically in environmental monitoring and food safety. Such selected research areas that should be accorded more attention in dealing with the challenge of toxin-producing microorganisms include:

1. **Climate change**: Considering ocean temperature changes, in addition to shifting nutrient profiles, it is important to learn how changes in the future will affect marine bacteria and algae distributions and their toxicity. Indeed, it has been noted that climate change mediates harmful algal bloom distribution, frequency, and intensity, as well as bacterial outbreaks. Changes in pH, temperature, and nutrient cycling might

alter the toxin production patterns among species. These are the issues on which much future research will focus, especially predictive modeling necessary to managing toxin risk in a changing climate **(Berdalet *et al.*, 2015)**. Understanding their response to climatic variables will be critical in toxin producing microbes as efforts gear toward appropriate responses against these emerging environmental dangers.

2. **Refining predictive model**: Advanced predictive models could result in more effective pre-advance management actions based on environmental parameters of HABs and bacterial bloom forecasts.
3. **Innovative control strategies**: New approaches to the control of toxin-producing microbes include microbial antagonism, genetic modification, or biotechnological applications and can thus be promising strategies that may reduce marine contamination and, subsequently, public health burdens.

9. Real-time monitoring and sustainable management

Real-time monitoring systems and biosensors are currently under development to become important tools in the finding of toxin-producing microorganisms within marine environments. These help in the identification of harmful blooms with enough time, which is greatly valued by stakeholders because timely interventions can be carried out effectively, reducing the impact on fisheries and public health. According to **Scholin (2019)**, such tools, when integrated within sustainable management frameworks, have the potential to reduce risks of seafood contamination and to enhance environmental monitoring. Environmental DNA (eDNA) technology has emerged as a reliable method for monitoring toxin-producing microorganisms in aquatic environments. By collecting water samples and analyzing DNA fragments, eDNA allows for the detection and quantification of harmful microalgal and bacterial species without the need for isolation or culture **(Xie *et al.*, 2023)**. Furthermore, biosensors enable real-time monitoring of toxins in water bodies, facilitating effective early warnings for harmful algal bloom (HAB) events or other contamination incidents **(Moore *et al.*, 2021)**. These technologies further enhance the capability to trace outbreaks of toxins and to advise efforts on the maintenance of public health and environmental management.

CONCLUSION

The huge ecological and health consequences of the increase of toxin-producing bacteria and microalgae in marine ecosystems are also related to their broad genetic, environmental, and ecological variability. This variability affects toxin types and production levels and the conditions under which toxins are produced. Omics, gene editing, and real-time monitoring do indeed finally allow enormous value in grasping the risks of these organisms and in enabling their management. These advances reaffirm the need for integrated, multi-disciplinary approaches to manage the ecological and health risks of toxin-producing microorganisms. By addressing the genetic, environmental, and technological aspects of toxin production, researchers can make valuable contributions to safer seafood products, healthier marine environments, and improved public health protections. Future studies should, therefore, try to refine predictive models of toxin outbreaks under changing environmental conditions in the light of climate change that affects ecosystems and can potentially influence toxin production. Further investigations into genetic pathways and adaptive mechanisms across diverse species can reveal additional new strategies toward toxins management in a sustainable way.

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REFERENCES

Accoroni, S.; Glibert, P.M.; Pichierri, S.; Romagnoli, T.; Marini, M. and Totti, C. (2015). A conceptual model of annual *Ostreopsis cf. ovata* blooms in the Northern Adriatic Sea based on the synergic effects of hydrodynamics, temperature, and the N:P ratio of water column nutrients. *Harmful Algae*, **45**: 14–25.

Allaf, M.M. (2023). *Heterosigma akashiwo*, a fish-killing flagellate. *Microbiol. Res.*, **14**(1): 132–147.

Alvarez, S.; Brown, C.E.; Diaz, M.G.; O'Leary, H. and Solís, D. (2024). Non-linear impacts of harmful algae blooms on the coastal tourism economy. *J. Environ. Manag.*, **351**: 1–12.

Amaro, H.M.; Salgado, E.M.; Nunes, O.C.; Pires, J.C.M. and Esteves, A.F. (2023). Microalgae systems - environmental agents for wastewater treatment and further potential biomass valorisation. *J. Environ. Manag.*, **337**.

Amin, S.A.; Parker, M.S. and Armbrust, E.V. (2012). Interactions between diatoms and bacteria. *Microbiol. Mol. Biol. Rev.*, **76**(3): 667–684.

Anderson, D.M. (2009). Approaches to monitoring, control and management of harmful algal blooms (HABs). *Ocean Coast. Manag.*, **52**(7): 342–347.

Bates, S.S.; Hubbard, K.A.; Lundholm, N.; Montresor, M. and Leaw, C.P. (2018). *Pseudo-nitzschia*, *Nitzschia*, and domoic acid: new research since 2011. *Harmful Algae*, **79**: 3–43.

Berdalet, E.; Fleming, L.E.; Gowen, R.; Davidson, K.; Hess, P. and Backer, L.C. (2015). Marine harmful algal blooms, human health and wellbeing: challenges and opportunities in the 21st century. *J. Mar. Biol. Assoc. UK*, **2015**: 1–64.

Blanco, J.; Martin, H.; Marino, C. (2017). Reduction of diarrhetic shellfish poisoning (DSP) toxins accumulation in cultured mussels by means of rope clustering and hydrodynamic barriers. *Aquaculture*, **479**: 1–17.

Blondeau-Patissier, D.; Gower, J.F.R.; Dekker, A.G.; Phinn, S.R. and Brando, V.E. (2014). A review of ocean color remote sensing methods and statistical techniques for the detection, mapping and analysis of phytoplankton blooms in coastal and open oceans. *Prog. Oceanogr.*, **123**: 123–144.

Bueno, E.; Pinedo, V. and Cava, F. (2020). Adaptation of *Vibrio cholerae* to Hypoxic Environments. *Front. Microbiol.*, **11**: 1–12.

Bui, Q.T.N.; Pradhan, B.; Kim, H.-S. and Ki, J.S. (2024). Environmental factors modulate saxitoxins (STXs) production in toxic Dinoflagellate *Alexandrium*: an updated review of STXs and synthesis gene aspects. *Toxins*, **16**(5): 210.

California Ocean Science Trust. (2016). Harmful algal blooms and California fisheries: frequently asked questions.

Cembella, A. and John, U. (2006). Molecular physiology of toxin production and growth regulation in harmful algae. In *Ecology of Harmful Algae* (pp. 215–227). Springer.

Cembella, A.D. (2003). Chemical ecology of eukaryotic microalgae in marine ecosystems. *Phycologia*, **42**(4): 420–447.

Centers for Disease Control and Prevention (CDC). (2019). Paralytic shellfish poisoning associated with eating shellfish — Alaska, May–June 2018. *MMWR Morb. Mortal. Wkly. Rep.*, **68**(3): 62–66.

Chorus, I. and Welker, M. (2021). Cyanobacterial toxins in drinking water: Occurrence, impacts, and treatment. *Toxins*, **13**(3): 153.

Cirri, E. and Pohnert, G. (2019). Algae−bacteria interactions that balance the planktonic microbiome. *New Phytol.*, **223**(1): 100–106.

D'Agostino, P.M.; Woodhouse, J.N.; Makower, A.K.; Yeung, A.C.; Ongley, S.E. and Micallef, M.L. (2016). Advances in genomics, transcriptomics and proteomics of toxin-producing cyanobacteria. *Environ. Microbiol. Rep.*, **8**(1): 3–13.

Daniels, N.A.; MacKinnon, L.; Bishop, R.; Altekruse, S.; Ray, B. and Hammond, R.M. (2000). *Vibrio parahaemolyticus* infections in the United States, 1973–1998. *J. Infect. Dis.*, **181**(5): 1661–1666.

Dhokane, D.; Shaikh, A.; Yadav, A.; Giri, N.; Bandyopadhyay, A. and Dasgupta, S. (2023). CRISPR-based bioengineering in microalgae for production of industrially important biomolecules. *Front. Bioeng. Biotechnol.*, **2023**: 1–15.

Dobrindt, U.; Hochhut, B.; Hentschel, U. and Hacker, J. (2004). Genomic islands in pathogenic and environmental microorganisms. *Nat. Rev. Microbiol.*, **2**(5): 414–424.

Faruque, S.M. and Nair, G.B. (2002). Molecular ecology of toxigenic *Vibrio cholerae*. *Microbiol. Mol. Biol. Rev.*, **66**(3): 454–478.

Flewelling, L.J.; Naar, J.P.; Abbott, J.P.; Baden, D.G.; Barros, N.B. and Bossart, G.D. (2005). Brevetoxicosis: red tides and marine mammal mortalities. *Nature*, **435**(7043): 755–756.

Garcia-Villada, L.; Rico, M.; Altamirano, M.; Sanchez-Martin, L.; Lopez-Rodas, V. and Costas, E. (2004). Occurrence of copper-resistant mutants in the toxic cyanobacteria *Microcystis aeruginosa*: characterisation and future implications in the use of copper sulfate as algaecide. *Water Res.*, **38**(8): 2207–2213.

Gogarten, J.P.; Doolittle, W.F. and Lawrence, J.G. (2002). Prokaryotic evolution in light of gene transfer. *Mol. Biol. Evol.*, **19**(12): 2226–2238.

Granéli, E. and Johansson, N. (2003). Effects of *Prymnesium parvum* Blooms on the aquatic ecosystem. *Phycologia*, **42**(4): 420–427.

Greenemeier, L. (2017). A mysterious killer alga just got a little less puzzling. *Wired Magazine*.

Griffith, A.W. and Gobler, C.J. (2020). Harmful algal blooms: A climate change co-stressor in marine and freshwater ecosystems. *Harmful Algae*, **2020**: 1–12.

Grossart, H.P. and Rojas-Jimenez, K. (2016). Aquatic fungi: targeting the forgotten in microbial ecology. *Curr. Opin. Microbiol.*, **31**: 140–145.

Hallegraeff, G.M. (2010). Ocean climate change, phytoplankton community responses, and harmful algal blooms: a formidable predictive challenge. *J. Phycol.*, **46**(2): 220–235.

Heisler, J.; Glibert, P.M.; Burkholder, J.M.; Anderson, D.; Cochlan, W. and Dennison, W. (2008). Eutrophication and harmful algal blooms: a scientific consensus. *Harmful Algae*, **8**(1): 3–13.

Horseman, M.A. and Surani, S. (2011). A comprehensive review of *Vibrio vulnificus*: an important cause of severe sepsis and skin and soft-tissue infection. *Int. J. Infect. Dis.*, **15**(3): e157–e166.

Janda, J.M. and Abbott, S.L. (2014). The genus *Shewanella*: from the brackish-water species to clinical pathogens. *Clin. Microbiol. Rev.*, **23**(4): 767–794.

Jeong, H.J.; Lim, A.S.; Lee, K.; Lee, M.J.; Seong, K.A. and Kang, N.S. (2017). Ichthyotoxic *Cochlodinium polykrikoides* red tides offshore in the South Sea, Korea in 2014: I. Temporal variations in three-dimensional distributions of red-tide organisms and environmental factors. *Algae*, **32**(2): 101–130.

Khan, S.; Arakawa, O. and Onoue, Y. (1996). A toxicological study of the marine phytoflagellate *Chattonella antiqua* (Raphydophyceae). *Phycologia*, **35**(3): 239–244.

Lan, J.; Liu, P.; Hu, X. and Zhu, S. (2024). Harmful algal blooms in eutrophic marine environments: causes, monitoring, and treatment. *Water*, **16**(17): 1–64.

Lan, W.; Wu, Y.; Han, L.; Wang, W.; Zhang, H. and Qin, B. (2024). Nutrient management and ecological restoration reduce the risk of harmful algal blooms in eutrophic lakes: Evidence from long-term monitoring and field experiments. *Water Res.*, **250**: 120303.

Landsberg, J.H. (2002). The effects of harmful algal blooms on aquatic organisms. *Rev. Fish. Sci.*, **10**(2): 113–390.

Larsson, M.E.; Laczka, O.F.; Harwood, D.T.; Lewis, R.J.; Himaya, S.W.A. and Murray, S.A. (2018). Toxicology of *Gambierdiscus* spp. (Dinophyceae) from tropical and temperate Australian waters. *Mar. Drugs*, **16**(1): 1–19.

Lee, J.; Lee, S. and Jiang, X. (2017). Cyanobacterial toxins in freshwater and food: important sources of exposure to humans. *Annu. Rev. Food Sci. Technol.*, **8**: 281–304.

Letchumanan, V.; Chan, K.G. and Lee, L.H. (2015). *Vibrio parahaemolyticus*: A review on the pathogenesis, prevalence, and advances in diagnosis and detection. *Front. Microbiol.*, **6**: 1–13.

Lewis, R.J. and Holmes, M.J. (1993). Ciguatera: human poisoning caused by marine biotoxins. *Toxicon*, **31**(6): 667–682.

Li, C.; Yao, Y.; Liu, X.; Chen, H.; Li, X. and Zhao, M. (2023). Integrated metabolomics, transcriptomics, and proteomics analyses reveal co-exposure effects of polycyclic aromatic hydrocarbons and cadmium on ryegrass (*Lolium perenne* L.). *Environment International*, **178**.

Maltsev, Y.; Kulikovskiy, M. and Maltseva, S. (2023). Nitrogen and phosphorus stress as a tool to induce lipid production in microalgae. *Microb. Cell Fact.*, **22**(239): 1–22.

Martin, J.F.; Kalcic, M.M.; Aloysius, N.; Apostel, A.M.; Brooker, M.R. and Evenson, G. (2021). Evaluating management options to reduce Lake Erie algal blooms using an ensemble of watershed models. *J. Environ. Manage.*, **280**: 1–10.

Matthews, M.W. (2014). Eutrophication and cyanobacterial blooms in South African inland waters: 10 years of MERIS observations. *Remote Sens. Environ.*, **155**: 161–177.

McCabe, R.M.; Hickey, B.M. and Trainer, V.L. (2023). The Pacific Northwest harmful algal blooms bulletin. *Harmful Algae*, **127**: 2023.

Merel, S.; Walker, D.; Chicana, R.; Snyder, S.; Baurès, E. and Thomas, O. (2013). State of knowledge and concerns on cyanobacterial blooms and cyanotoxins. *Environ. Int.*, **59**: 303–327.

Michalak, A.M.; Anderson, E.J.; Beletsky, D.; Boland, S.; Bosch, N.S. and Bridgeman, T.B. (2013). Record-setting algal bloom in Lake Erie caused by agricultural and meteorological trends consistent with expected future conditions. *PNAS*, **110**(16): 6448–6452.

Montero, D.A.; Vidal, R.M.; Velasco, J.; George, S.; Lucero, Y. and Gómez, L.A. (2023). *Vibrio cholerae*, classification, pathogenesis, immune response, and trends in vaccine development. *Front. Med. (Lausanne)*, **10**: 1–24.

Montuori, E.; De Luca, D.; Penna, A.; Stalberga, D. and Lauritano, C. (2023). *Alexandrium* spp.: From Toxicity to Potential Biotechnological Benefits. *Mar. Drugs*, **22**(1): 31.

Moore, S.K.; Mickett, J.B.; Doucette, G.J.; Adams, N.G.; Mikulski, C.M. and Birch, J.M. (2021). An Autonomous Platform for Near Real-Time Surveillance of Harmful Algae and Their Toxins in Dynamic Coastal Shelf Environments. *J. Mar. Sci. Eng.*, **9**: 336.

Moore, T.S.; Campbell, J.W. and Dowell, M.D. (2009). A class-based approach to characterizing and mapping the uncertainty of the MODIS ocean chlorophyll product. *Remote Sens. Environ.*, **113**(11): 2424–2430.

Moss, B.; Stephen, D.; Alvarez, C.; Becares, E.; van de Bund, W. and Collings, S.E. (2003). The determination of ecological quality in shallow lakes—a tested system (ECOFRAME) for implementation of the European Water Framework Directive. *Aquat. Conserv.: Mar. Freshw. Ecosyst.*, **6**(2): 107–126.

Nakamura, Y.; Ito, K. and Sato, T. (2020). Influence of environmental stress on toxin production by marine bacteria. *Appl. Environ. Microbiol.*, **86**(15): e00934-20.

National Aeronautics and Space Administration (NASA). (2016). Florida’s 2016 toxic algae bloom. *NASA Earth Observatory*.

National Oceanic and Atmospheric Administration (NOAA). (2015). West coast harmful algal bloom. *US Department of Commerce*; Accessed June 2, 2025.

Neilan, B.A.; Pearson, L.A.; Muenchhoff, J.; Moffitt, M.C. and Dittmann, E. (2013). Environmental conditions that influence toxin biosynthesis in cyanobacteria. *Environ. Microbiol.*, **15**(5): 1239–1253.

Ng, W.L. and Bassler, B.L. (2009). Bacterial quorum-sensing network architectures. *Annu. Rev. Genet.*, **43**: 197–222.

Oda, T.; Nakamura, A.; Shikayama, M.; Kawano, I.; Ishimatsu, A. and Muramatsu, T. (1997). Generation of reactive oxygen species by raphidophycean phytoplankton. *Biosci. Biotechnol. Biochem.*, **61**(10): 1658–1662.

Paerl, H.W.; Hall, N.S. and Calandrino, E.S. (2011). Controlling harmful cyanobacterial blooms in a world experiencing anthropogenic and climatic-induced change. *Sci. Total Environ.*, **409**(10): 1739–1745.

Paerl, H.W.; Otten, T.G. and Kudela, R. (2018). Mitigating the expansion of harmful algal blooms across the freshwater-to-marine continuum. *Environ. Sci. Technol.*, **50**(17): 8365–8373.

Paerl, H.W.; Scott, J.T.; McCarthy, M.J.; Newell, S.E.; Gardner, W.S. and Havens, K.E. (2016). It takes two to tango: When and where dual nutrient (N & P) reductions are needed to protect lakes and downstream ecosystems. *Environ. Sci. Technol.*, **50**(20): 10805–10813.

Pearson, L.A. and Neilan, B.A. (2008). The molecular genetics of cyanobacterial toxicity as a basis for monitoring water quality and public health risk. *Curr. Opin. Biotechnol.*, **19**(3): 281–288.

Peck, M.W. (2006). *Clostridium botulinum* and the safety of minimally heated, chilled foods: an emerging issue? *J. Appl. Microbiol.*, **101**(3): 556–570.

Pezzolesi, L.; Pistocchi, R.; Fratangeli, F.; Dell'Aversano, C. and Tartaglione, L. (2014). Growth dynamics in relation to the production of the main cellular components in the toxic Dinoflagellate *Ostreopsis cf. ovata*. *Harmful Algae*, **36**: 1–10.

Pezzolesi, L.; Vanucci, S.; Dell'Aversano, C.; Dello Iacovo, E.; Tartaglione, L. and Pistocchi, R. (2016). Effects of N and P availability on carbon allocation in the toxic Dinoflagellate *Ostreopsis cf. ovata*. *Harmful Algae*, **55**: 202–212.

Pierce, R.H. and Henry, M.S. (2008). Harmful algal toxins of the Florida red tide (*Karenia brevis*): natural chemical stressors in South Florida coastal ecosystems. *Ecotoxicology*, **17**(7): 623–631.

Pirazzini, M.; Montecucco, C. and Rossetto, O. (2022). Toxicology and pharmacology of botulinum and tetanus neurotoxins: an update. *Arch. Toxicol.*, **96**(6): 1521–1539.

Pulido, O.M. (2016). Phycotoxins by harmful algal blooms (HABS) and human poisoning: an overview. *Int. Clin. Pathol. J.*, **2**(6): 145–152.

Ramanan, R.; Kim, B.H.; Cho, D.H.; Oh, H.M. and Kim, H.S. (2016). Algae–bacteria interactions: Evolution, ecology and emerging applications. *Biotechnol. Advan.*, **34**(1): 14–29.

Ritchie, J.M. and Waldor, M.K. (2009). The thermostable direct hemolysin of *vibrio parahaemolyticus*: a pore-forming toxin with a repertoire of host cell effects. *J. Bacteriol.*, **191**(13): 4001–4009.

Rivas, A.J.; Vences, A.; Husmann, M.; Lemos, M.L. and Osorio, C.R. (2015). *Photobacterium damselae* subsp. *damselae* major virulence factors Dly, plasmid-encoded HlyA, and chromosome-encoded HlyA are secreted via the type II secretion system. *Infect. Immun.*, **83**(4): 1246–1256.

Rutherford, S.T. and Bassler, B.L. (2012). Bacterial Quorum sensing: its role in virulence and possibilities for its control. *Cold Spring Harb. Perspect. Med.*, **2**(11): a012427.

Sampaio, A.; Silva, V.; Poeta, P. and Aonofriesei, F. (2022). *Vibrio* spp.: life strategies, ecology, and risks in a changing environment. *Diversity*, **14**(97): 1–26.

Schmidt, G. (2024). Some examples of bacterial toxins as tools. *Toxins*, **16**(5): 1–13.

Scholin, C.A. (2019). Molecular approaches to detecting harmful algal blooms. *Harmful Algae*, **84**: 103–112.

Scholin, C.A.; Doucette, G.J.; Jensen, S.; Roman, B.; Pargett, D. and Marin, R. (2009). Remote detection of marine microbes, small invertebrates, harmful algae, and biotoxins using the environmental sample processor (ESP). *Oceanogr.*, **22**(2): 158–167.

Schuijt, L.M.; Peng, F.J.; van den Berg, S.J.P.; Dingemans, M.M.L. and Van den Brink, P.J. (2021). (Eco)toxicological tests for assessing impacts of chemical stress to aquatic ecosystems: Facts, challenges, and future. *Sci. Tot. Environ.*, **795**: 1–18.

Selander, E.; Thor, P.; Toth, G. and Pavia, H. (2019). Copepods drive large-scale trait-mediated effects in marine plankton. *Sci. Adv.*, **5**(4): 1–6.

Seyedsayamdost, M.R.; Chandler, J.R.; Blodgett, J.A.V.; Lima, P.S.; Duerkop, B.A.; Oinuma, K. et al. (2010). Quorum-sensing-regulated bactobolin production by *Burkholderia thailandensis* E264. *ACS Chem. Biol.*, **6**(12): 1277–1286.

Sharpley, A.N.; Kleinman, P.J.A.; Flaten, D.N. and Buda, A.R. (2006). Critical source area management of agricultural phosphorus: experiences, challenges and opportunities. *Water Sci. Technol.*, **53**(2): 21–28.

Sheahan, M.; Gould, C.A.; Neumann, J.E.; Kinney, P.L.; Hoffmann, S. and Fant, C. (2022). Examining the relationship between climate change and vibriosis in the United States: projected health and economic impacts for the 21st century. *Environ. Health. Perspect.*, **130**(8): 1–13.

Smayda, T.J. (2008). Patterns of variability characterizing marine phytoplankton, with examples from Narragansett Bay. *ICES J. Mar.Sci.*, **65**(6): 735–739.

Solé, J.; Estrada, M. and García-Ladona, E. (2006). Biological control of harmful algal blooms: A modelling study. *J. Marine Syst.*, **61**(3): 165–179.

Steffen, M.M.; Belisle, B.S.; Watson, S.B.; Boyer, G.L. and Wilhelm, S.W. (2014). Status, causes and controls of cyanobacterial blooms in Lake Erie. *J. Great Lakes Res.*, **40**(2): 215–225.

Tang, Y.Z. and Gobler, C.J. (2009). Characterization of the toxicity of *Cochlodinium polykrikoides* isolates from Northeast US estuaries to finfish and shellfish. *Harmful Algae*, **8**(3): 454–462.

Trainer, V.L. and Hardy, F.J. (2015). Integrative Monitoring of Marine and Freshwater Harmful Algae in Washington State for Public Health Protection. *Toxins*, **7**(4): 1206–1234.

Tulatz, S.; Krock, B.; Tillmann, U. and Meunier, C.L. (2024). Effects of temperature, salinity and CO_2 concentration on growth and toxin production of the harmful algal bloom species *Alexandrium pseudogonyaulax* (Dinophyceae) from the Danish Limfjord. *Harmful Algae*, **140**: 1–11.

U.S. Environmental Protection Agency (EPA). (2015). Lake Erie harmful algal bloom—Toledo, Ohio 2014. *Washington, DC: U.S. EPA.*

U.S. Environmental Protection Agency (EPA). (2019). Recommendations for cyanobacteria and cyanotoxins in recreational waters. *EPA-822-R-19-001*.

United States Environmental Protection Agency (EPA). (2016). Harmful algal blooms and drinking water: cyanobacteria and cyanotoxins. *EPA*.

Valério, E.; Chaves, S. and Tenreiro, R. (2010). Diversity and impact of prokaryotic toxins on aquatic environments: a review. *Toxins (Basel)*, **2**(10): 2359–2410.

Vidyarathna, N.K. and Granéli, E. (2013). Physiological responses of *Ostreopsis ovata* to changes in N and P availability and temperature increase. *Harmful Algae*, **21–22**: 54–63.

Vila, M.; Herràndiz, R.A.; Fontanet, J.I.; Alvarez, J. and Berdalet, E. (2001). Establishing the link between *Ostreopsis cf. Ovata* blooms and human health impacts using ecology and epidemiology. *Sci. Mar.*, **80**(S1): 107–115.

Wolfe, G.V. (2000). The chemical defense ecology of marine unicellular plankton: constraints, mechanisms, and impacts. *Biol. Bull.*, **198**(2): 225–244.

Xie, Y.; DeBeer, C. and Giesy, J.P. (2023). eDNA for aquatic ecosystem monitoring. *Global Water Futures. University of Saskatchewan*.

Zheng, D.; Yin, G.; Liu, M.; Chen, C.; Jiang, Y. and Hou, L. (2021). A systematic review of antibiotics and antibiotic resistance genes in estuarine and coastal environments. *Sci. Total Environ.*, **777**: 1–17.