PNAS COMMENTARY

Molecular forecasting of toxic bloom events

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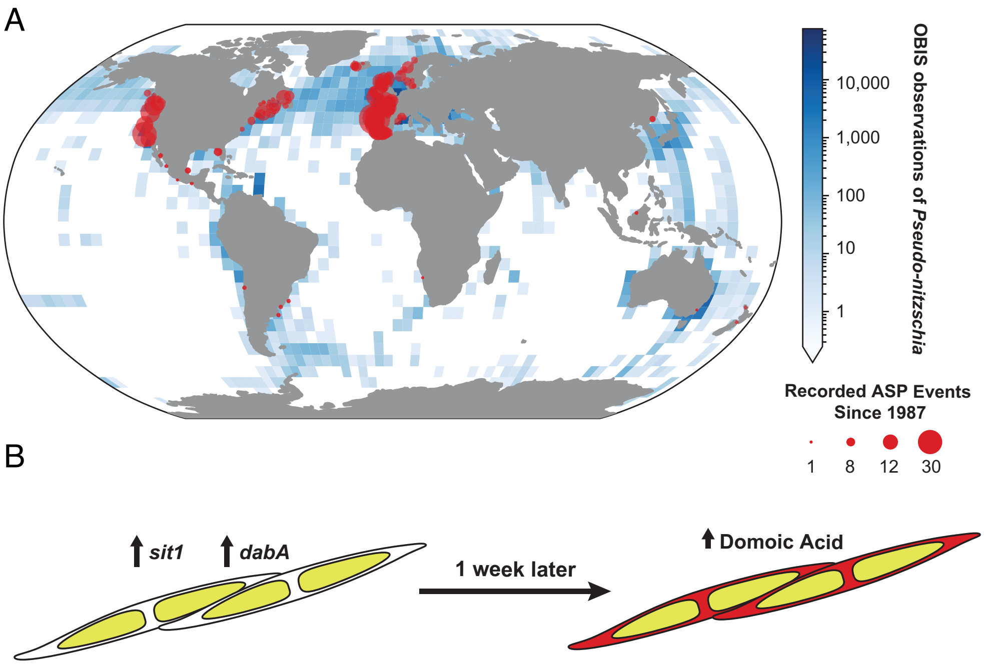

Fig. 1. *Pseudo-nitzschia* is a cosmopolitan diatom genus with many species capable of producing domoic acid, a neurotoxin which causes Amnesic Shellfish Poisoning. (*A*) The occurrence of *Pseudo-nitzschia* is plotted based on observations recorded by the Ocean Biodiversity Information System (OBIS) (9). The localization of Amnesiac Shellfish Poisoning (ASP) events reported since 1987 is highlighted in red circles, with the size of the circle corresponding to the number of reported events in a given region based on data from the Harmful Algal Bloom Event Database (HAEDAT) (10). (*B*) The metatranscriptomic model proposed by Brunson et al. wherein the expression of silicon transporter (*sit1*) and the domoic acid biosynthesis gene (*dabA*) can predict enhanced domoic acid a week in advance of the event.

In 2015, a harmful algal bloom (HAB) of the toxin-producing alga *Pseudo-nitzschia australis* stretched the length of the North American west coast from Santa Barbara, California, to the Aleutian Islands. The bloom was both the largest and longest HAB recorded in the region and was accompanied by exceptionally high levels of domoic acid (1), a neurotoxin that can bioaccumulate in seafood and cause potentially lethal amnesic shellfish poisoning in humans and mortality in marine mammals and other megafauna (2). The remarkable extent of this bloom coincided with a regional physical anomaly, the northeast Pacific "warm blob" (3), but seasonal blooms of toxic and nontoxic *Pseudo-nitzschia* species have long been observed to bloom in response to coastal upwelling conditions in the region (4). Predicting and understanding the drivers of these toxic events is central to our ability to respond to them and may be important in preventing or mitigating HABs in the future. In this issue of PNAS, Brunson et al. (5) integrated high-resolution metatranscriptomic data collected in tandem with local monitoring efforts in Monterey Bay, CA during the 2015 HAB event to identify the drivers of bloom formation and domoic acid production. Their work uncovers the likely colimitation of *P. australis* by silica and iron and identifies gene targets that may enable the prediction of toxin-producing HABs a week in advance of the production.

As with land plants, the growth dynamics of phytoplankton, the small photosynthetic microbes that drive primary production in the ocean, are governed by the physical and chemical environment as well as biological interactions. Both bottom–up (e.g., the supply of nutrients like nitrogen, phosphorus, and iron) and top–down (e.g., grazing or viral lysis) controls on phytoplankton growth are central to determining the primary productivity and the dominant and successful taxa within a region. Anthropogenic warming, rising CO_2, increasing stratification, and changes in nutrient supply are anticipated to alter the patterns of productivity and dominant taxa across ecosystems—including changing the ranges and bloom frequencies of HAB-forming species like *Pseudo-nitzschia* (6, 7). *Pseudo-nitzschia* is a globally distributed (Fig. 1) genus of diatoms (class Bacillariophyceae) that encompasses over 50 distinct species, half of which have been found to be toxigenic (like *P. australis*) and capable of producing domoic acid (8).

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The California Current System, which runs along the west coast of North America is an eastern boundary system where wind drives the upwelling of cold, waters rich in nutrients to the surface. Phytoplankton thrive in these nutrient-rich waters and form the base of the marine food web, supporting diverse populations of fish, seabirds, and marine mammals. Diatoms, including *Pseudo-nitzschia*, are often the first to bloom during upwelling events as they are adapted to capitalize on the availability of high concentrations of nutrients and rapidly draw them down (11). Diatoms are unique among algae in their physiological requirements for silica, which they use to construct a silica frustule—a glass casing that encapsulates the cell. During the 2015 *P. australis* bloom, silica concentrations in the Monterey Bay fell far below those of nitrate, suggesting that the bloom may have been constrained by silica limitation (1).

In PNAS, Brunson et al. integrated high-resolution metatranscriptomic data collected in tandem with local monitoring efforts in Monterey Bay, CA, to identify the drivers of bloom formation and domoic acid production.

Metatranscriptomics, or the sequencing of the total community messenger RNA (mRNA), a type of RNA that carries the information needed to make proteins, has been used with great success to better understand the drivers and nutritional physiology of bot toxic and nontoxic phytoplankton blooms across marine ecosystems (12, 13). Building off laboratory-based studies of phytoplankton isolates, a variety of nutrient-responsive genes have been identified that may help identify and characterize patterns of nutrient stress in natural populations. Brunson et al. (5) conducted extensive weekly metatranscriptomic sampling that enabled them to directly assess and track the progression of the physiological state of *P. australis* over the course of the bloom. Their molecular investigation confirmed likely silica limitation (through high expression of silicon transporter *sit1*) but also found evidence of concurrent iron limitation (through high expression of iron stress induced protein (ISIP)). *Pseudo-nitzschia* is known to be a good competitor in low-iron conditions (14), which may have enabled it to succeed and out compete other diatoms during the upwelling event in 2015.

Domoic acid was first identified as produced by diatoms following a 1987 poisoning event on Prince Edward Island, which led to three deaths (15). Yet, it was not until 2018 that the biosynthetic pathway for domoic acid (the *dab* gene cluster) was characterized in *Pseudo-nitzschia multiseries* by Brunson et al. (16). In their 2018 paper, they additionally suggested that *dabA*, a terpene cyclase that catalyzes the first step of the synthesis domoic acid from gernyal pyrophosphate and L-glutamic acid, may be an ideal transcriptional target for environmental monitoring of domoic acid production as it is apparently phylogenetically constrained to *Pseudo-nitzschia* and only found within the transcriptome assemblies of toxic strains (16). In this issue of PNAS, Brunson et al. (many of whom were involved the discovery of the *dab* gene cluster) used the metatranscriptomic data to recover novel transcripts from the *dab* gene cluster from multiple *Pseudo-nitzschia* species (5). They then tracked these transcripts over the course of the bloom, finding that the expression of *dabA* coincided with periods of enhanced domoic acid production. But the outcome from this study which is most promising from a monitoring standpoint was a model which found that the increased expression of *dabA* and the silicon transporter *sit1* predicted toxicity with high accuracy a week in advance of the event.

The work by Brunson et al. beautifully demonstrates the ecological insights that can be made by integrating metatranscriptomics into a local HAB monitoring program, like identifying the likely underlying importance of iron supply in the 2015 bloom (5). Though powerful, it is currently expensive and computationally impractical to propose to apply global molecular methods like metatranscriptomics broadly for management or surveillance of HABs. However, the direct measurement of the expression of one or two genes, such as *dabA* and *sit1* shown here, may be more readily adopted by stakeholders to monitor local ecosystems. Moreover, this direct monitoring of targeted gene expression could be deployed on automated in situ platforms like the Environmental Sample Processor (17) as a means of forecasting toxic events. As temperatures across the globe continue to change, shifting patterns of ocean circulation, nutrient supply, and the ranges and phenology of HABs (18, 19), our understanding of the molecular underpinnings of HABs is paramount to our ability to respond to and predict these toxic events (20).

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1. J. P. Ryan *et al.*, Causality of an extreme harmful algal bloom in Monterey Bay, California, during the 2014–2016 northeast Pacific warm anomaly. *Geophys. Res. Lett.* **44**, 5571–5579 (2017).
2. V. L. Trainer *et al.*, *Pseudo-nitzschia* physiological ecology, phylogeny, toxicity, monitoring and impacts on ecosystem health. *Harmful Algae* **14**, 271–300 (2012).
3. R. M. McCabe *et al.*, An unprecedented coastwide toxic algal bloom linked to anomalous ocean conditions. *Geophys. Res. Lett.* **43**, 10366–10376 (2016).
4. J. Smith *et al.*, A decade and a half of *Pseudo-nitzschia* spp. and domoic acid along the coast of southern California. *Harmful Algae* **79**, 87–104 (2018).
5. J. K. Brunson *et al.*, Molecular forecasting of domoic acid during a pervasive toxic diatom bloom. *Proc. Natl. Acad. Sci. U.S.A.* **121**, e2319177121 (2024).
6. C. J. Gobler, Climate change and harmful algal blooms: Insights and perspective. *Harmful Algae* **91**, 101731 (2020).
7. S. K. Moore *et al.*, Impacts of climate variability and future climate change on harmful algal blooms and human health. *Environ. Health* **7**, S4 (2008).
8. S. S. Bates, K. A. Hubbard, N. Lundholm, M. Montresor, C. P. Leaw, *Pseudo-nitzschia*, *Nitzschia*, and domoic acid: New research since 2011. *Harmful Algae* **79**, 3–43 (2018).
9. OBIS, "Ocean biodiversity information system" (Intergovernmental Oceanographic Commission of UNESCO, 2024), obis.org. Accessed 3 September 2024.
10. P. Provoost, H. Enevoldsen, Harmful Algal Event Database (HAEDAT). IOC Harmful algal bloom programme. https://doi.org/10.25607/OWDRMQ. Accessed 3 September 2024.
11. R. Margalef, Life-forms of phytoplankton as survival alternatives in an unstable environment. *Oceanolog. Acta* **1**, 493–509 (1978).
12. H. Alexander, B. D. Jenkins, T. A. Rynearson, S. T. Dyhrman, Metatranscriptome analyses indicate resource partitioning between diatoms in the field. *Proc. Natl. Acad. Sci. U.S.A.* **112**, E2182–E2190 (2015).
13. A. Marchetti *et al.*, Comparative metatranscriptomics identifies molecular bases for the physiological responses of phytoplankton to varying iron availability. *Proc. Natl. Acad. Sci. U.S.A.* **109**, E317–E325 (2012).
14. R. H. Lampe *et al.*, Divergent gene expression among phytoplankton taxa in response to upwelling. *Environ. Microbiol.* **20**, 3069–3082 (2018).
15. S. S. Bates *et al.*, Pennate diatom *Nitzschia pungens* as the primary source of Domoic Acid, a toxin in shellfish from Eastern Prince Edward Island, Canada. *Can. J. Fish. Aquat. Sci.* **46**, 1203–1215 (1989).
16. J. K. Brunson *et al.*, Biosynthesis of the neurotoxin domoic acid in a bloom-forming diatom. *Science* **361**, 1356–1358 (2018).

17. C. Scholin *et al.*, Remote Detection of marine microbes, small invertebrates, harmful algae, and biotoxins using the Environmental Sample Processor (ESP). *Oceanography* **22**, 158–167 (2009).
18. D. M. Anderson *et al.*, Evidence for massive and recurrent toxic blooms of *Alexandrium catenella* in the Alaskan Arctic. *Proc. Natl. Acad. Sci. U.S.A.* **118**, e2107387118 (2021).
19. S. Clark *et al.*, *Pseudo-nitzschia* bloom dynamics in the Gulf of Maine: 2012–2016. *Harmful Algae* **88**, 101656 (2019).
20. G. M. M. Hennon, S. T. Dyhrman, Progress and promise of omics for predicting the impacts of climate change on harmful algal blooms. *Harmful Algae* **91**, 101587 (2020).