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Microcystin as a Biogeochemical Cycle: pools, fluxes, and fates of the cyanotoxin in inland waters

Quin K. Shingai[1,2] and Grace M. Wilkinson[1,3*]

[1]Department of Ecology, Evolution, and Organismal Biology, Iowa State University
[2]Current Address: Department of Biological Sciences, Dartmouth College
[3]Current Address: Center for Limnology, University of Wisconsin – Madison

*Corresponding Author: gwilkinson@wisc.edu

Shingai ORCiD: 0000-0002-7788-4233
Wilkinson ORCiD: 0000-0003-4051-2249

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Data Availability

Data Availability Statement: This is a literature synthesis from previously published data by other authors. The collated values from the literature and proper citation are in the Supporting Information S1. The calculated or collated values used in the analysis are available through the Environmental Data Initiative at doi:10.6073/pasta/0650f1cba18af503915e649f46e427e3. The code and tabulated values for models and figure generation can be found at doi:10.5281/zenodo.7434858.

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Scientific Significance Statement

There is a pressing need to understand the dynamics of microcystin, a toxin produced by some cyanobacteria, in the environment. Despite substantial advancements in our understanding of individual pools of microcystin, we lack a synthesized understanding of the sources, sinks, and movement of cyanotoxins within aquatic ecosystems. Using a literature synthesis approach, we developed a conceptual biogeochemical cycle of microcystin in lakes. We identified and synthesized the magnitude of four major pools of microcystin in lakes and reservoirs and nine major fluxes, including into the terrestrial environment (another major pool). Through this literature synthesis approach, we also identified understudied pools and fluxes. Adopting the framework of a 'microcystin cycle' can provide new insights for the management and mitigation of microcystin exposure risks.

Abstract

Microcystin poses a serious threat to aquatic ecosystems and human health. There is a pressing need to understand the production, movement, and storage of microcystin in lakes. We constructed a conceptual biogeochemical model for microcystin through a comprehensive literature synthesis, identifying four major pools and nine major fluxes in lakes that also connect to the terrestrial environment. This conceptual model can be used as the framework for developing ecosystem mass balances of microcystin. We propose that the concentration of microcystin in the water column is the balance between the import, sediment translocation, production and degradation, uptake, burial, and export. However, substantial unknowns remain pertaining to the magnitude and movement of microcystin. Future investigations should focus on sediment fluxes, drivers of biodegradation, and seasonal dynamics. Adopting the framework of a 'microcystin cycle' improves our understanding of processes driving toxin prevalence and helps to prioritize strategies for minimizing exposure risks.

Introduction

The widespread eutrophication of inland waters combined with a changing climate is modifying the magnitude and severity of cyanobacteria blooms in some, but not all, waterbodies (Ho et al. 2019; Wilkinson et al. 2022). Cyanobacteria blooms can pose a serious threat to aquatic ecosystems and public health, particularly through the production of toxins that have the capacity to disrupt ecosystem services. Cyanotoxins create unsafe conditions for recreational water use and impede provisioning services such as fisheries, irrigation, and drinking water supplies (Carmichael and Boyer 2016). While there are numerous cyanotoxins, microcystin is among the most prevalent in inland waters (Rastogi et al. 2014). Microcystins are a group of monocyclic heptapeptides produced by numerous genera of cyanobacteria in both marine and freshwater ecosystems. Given the ubiquity of this toxin, persistence in the environment, and the potential for severe harm to humans and wildlife, there is a pressing need to understand the dynamics of when, where, and how microcystin is produced, transformed, moves, and accumulates.

As microcystin produced in the water column is a key reservoir and pathway for human exposure, a major research focus has been documenting the incidence and magnitude of microcystin concentrations in the water column (Loftin et al. 2016) and the environmental

conditions that lead to microcystin production (Orihel et al. 2012; Harris et al. 2014). There has also been substantial effort to identify the organisms and processes that metabolize microcystin into less harmful molecules (Dziga et al. 2013; Schmidt et al. 2014; Massey and Yang 2020). Additionally, there has been effort to understand the accumulation, transformation, and movement of microcystin in the aquatic food web (Kozlowsky-Suzuki et al. 2012; Flores et al. 2018), sediments (Zastepa et al. 2015; Wood et al. 2020), and the terrestrial environment (Ibelings and Chorus 2007). However, despite substantial advancements in our understanding of these individual pools of microcystin, we lack a synthesized understanding of the sources, sinks, and movement of cyanotoxins within aquatic ecosystems.

Our objective was to develop a biogeochemical model for microcystin from an ecosystem perspective that synthesizes production, movement, and storage in lakes. While our focus here is on lakes, the conceptual model we propose is adaptable to other aquatic ecosystems, including both marine and freshwater environments. Conceptual models of biogeochemical cycles provide a framework for examining the transport and transformation of molecules within and among ecosystems, including the interactions between abiotic and biotic components of the ecosystem. In addition to the more common elemental cycles, biogeochemical frameworks have recently been used to study contaminants such as plastic pollution (Hoellein and Rochman 2021), revealing important pathways for future research. We used this conceptual model to synthesize the current knowledge of the magnitudes of microcystin pools and fluxes in lakes, revealing gaps in our understanding of microcystin dynamics. By taking a comprehensive literature-review approach, we have been able to identify which pools and fluxes are well studied in lakes and which dynamics have received less attention, despite being potentially important pathways for human exposure. Additionally, this conceptual framework can provide new insights for the management of microcystin exposure risks to humans and wildlife.

Constructing the Microcystin Cycle

To construct a comprehensive cycle of microcystin for inland waterbodies, specifically focusing on lakes, we reviewed and synthesized the current information on microcystin pools and fluxes in the literature. We performed a literature search in Web of Science using the terms "microcystin*" and "lake*", which returned 1781 articles. We supplemented this search with additional results by searching for "microcystin*" with "sediment*", "macrophyte*",

"degradation*", and "aerosol*". Each article's abstract was reviewed to determine if the study contained information pertinent to our synthesis goals and had measurements from an inland waterbody. For studies that were deemed potentially pertinent based on the abstract, the main text was reviewed and if a pool or flux was measured, the estimate of the magnitude was extracted along with details about the ecosystem and methods (see Supplementary tables). In most studies, the magnitude was reported as a range of measured concentrations. We then synthesized this information to estimate the range of microcystin concentrations, the fluxes into and out of each pool, compare the magnitude and rates to biomass turnover times, and identify any gaps in our understanding of the processes that control microcystin dynamics within the pool. In total, we synthesized the quantitative results from 160 studies (see Supplemental Information). While microcystin production and cycling also occurs in marine environments, we chose to limit the literature synthesis to lakes for this study (with some studies also reporting results for reservoirs). However, the conceptual microcystin cycle (pools and fluxes) that we constructed from this review is generally applicable across the aquatic continuum.

From our literature review, we identified four major pools of microcystin within lakes: *A. water column, B. sediment, C. macrophytes, and D. aquatic consumers* (letters correspond to major pools in Figure 1, Figure S1). Each of these major pools can be further divided into sub-pools based on the form (e.g., intercellular, extracellular in the water column and sediments) or trophic guild (e.g., zooplankton in aquatic consumers) that contribute to the dynamics in their major pools. These major pools are connected to each other and the *E. terrestrial environment* (another major pool with sub-pools) through nine major fluxes (numbered 1-9 in Figure 1). These fluxes can be broadly categorized as *cellular* fluxes including lysis and several forms of degradation, *food web* fluxes including consumption (direct ingestion or inhalation), excretion, and uptake (osmotic equilibration with biotic tissues), and *transport* fluxes including sedimentation, resuspension, aerosolization, and hydrologic import and export through surface and groundwater movement.

Based on this literature synthesis, we propose that concentrations of microcystin in the water column (the most frequently measured pool) are the balance between the import, translocation from the sediments, internal production of microcystin and the degradation, uptake, burial, and export of microcystin. In other words, water column concentrations are not reflective of intercellular microcystin production alone. Below, we describe each major pool including the

sub-pools and fluxes that connect them and the environmental conditions that drive accumulation or loss from each pool.

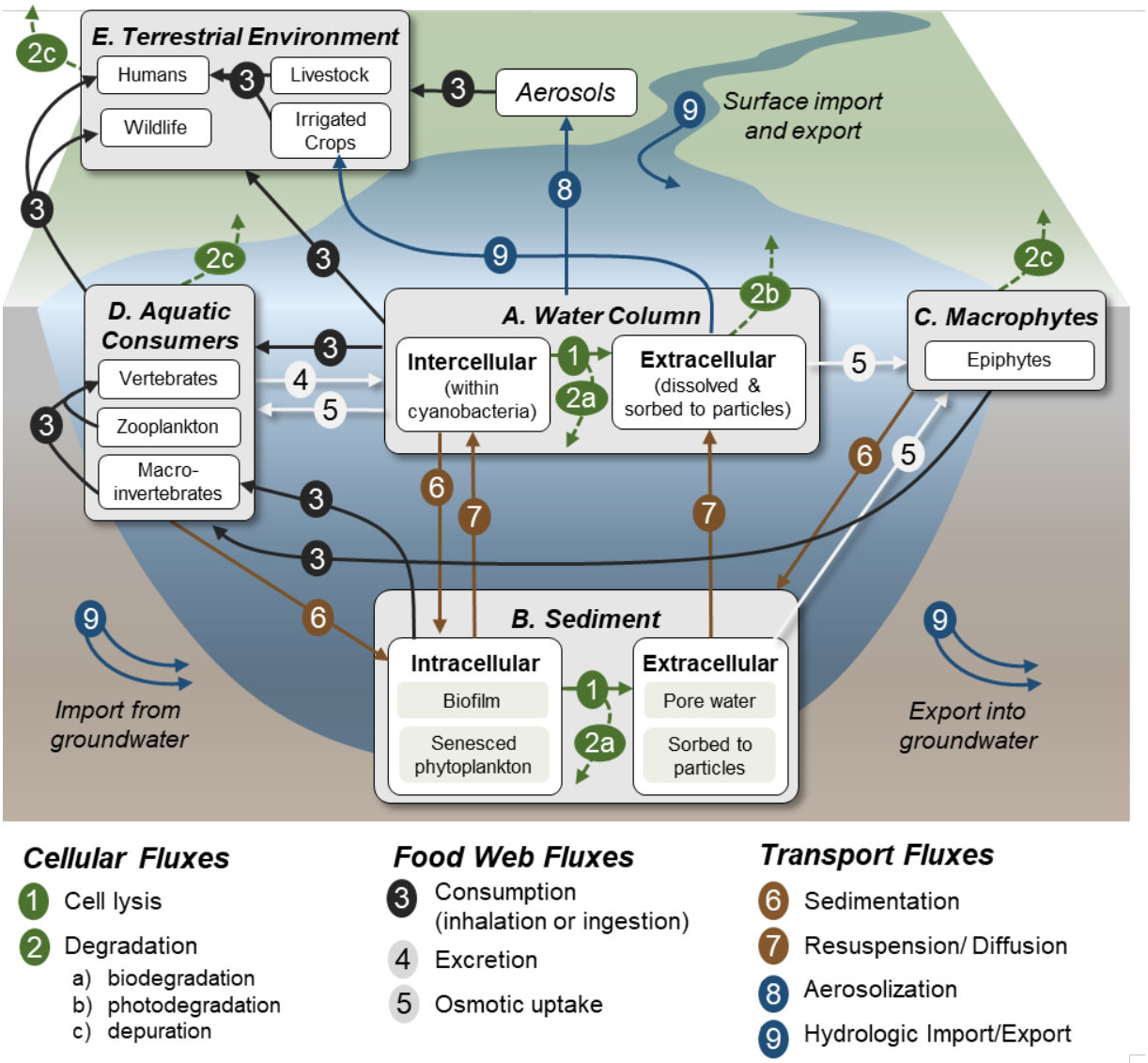

Figure 1. *A conceptual model of the microcystin cycle in lentic inland waters. The major pools (A-E) of microcystin and sub-pools (white boxes within major pools) are labeled in the diagram in light grey boxes. The major fluxes among these pools are denoted with the color-coded arrows. The numbers on the arrows correspond to the key of fluxes below the figure. The fluxes (arrows) are between the major pools and inclusive of all sub-pools unless arrows specifically connect two sub-pools (e.g., the diffusion flux [#7] between the extracellular sediment sub-pool and the extracellular water column sub-pool).*

A. Water Column Pool

Sub-Pools in the Water Column

Microcystin is synthesized within the vegetative cells of cyanobacteria, forming the intercellular pool of microcystin. When microcystin-producing cyanobacteria are blooming (experiencing exponential population growth), the pool of intercellular microcystin in the water column can increase if toxigenic strains dominate the assemblage. When cells are lysed or damaged, intercellular microcystin is released into the extracellular microcystin pool. In its extracellular form, microcystin can adsorb to particles and organic matter or be subject to further degradation and loss from the ecosystem due to ultraviolet radiation or bacterial metabolism (Munusamy et al. 2012; Massey and Yang 2020). High microcystin concentrations in lakes and reservoirs, reported as the intercellular, extracellular, or combined total concentrations, are associated with eutrophic conditions and low N:P ratios in the surface waters which favor cyanobacterial dominance (Orihel et al. 2012; Harris et al. 2014). Additionally, warmer water temperatures and greater water column stability are conditions that favor cyanobacterial blooms leading to higher microcystin concentrations in the water column (Mantzouki et al. 2018). However, given the dynamic nature of blooms, the size of the microcystin pool in the water column is also dynamic.

Assessing the likelihood that a measurable pool of microcystin is present in the water column is challenging given the dynamic nature of cyanobacteria blooms and other fluxes (Figure 1). Large, randomized surveys can provide a snapshot of microcystin pools among hundreds, or even thousands of lakes (Loftin et al. 2016), whereas longitudinal studies on a smaller number of waterbodies are more likely to capture brief episodes of toxin production. To quantify the incidence of a measurable microcystin pool in the water column of lakes and reservoirs, we compiled studies that reported surveying at least five waterbodies for microcystin concentrations. Surveys reported either intercellular, dissolved, or both concentrations combined for the water column. We used the information reported in these papers to calculate the percentage of waterbodies with detectable microcystin pools in the water column for each survey. In total, we reviewed 67 studies that reported on 69 surveys (Table S1). We did not discriminate among survey designs (e.g., statistically randomized, longitudinal, opportunistic); however, if microcystin was detected during any point in a repeated sampling design, the waterbody was considered to have detectable microcystin concentrations. We also categorized the frequency of sampling as reported in 62 of the survey as repeated (>2 sampling events in each waterbody) or snapshot (1-2 sampling events only in a waterbody). Ten of the studies did

not provide enough information to determine which waterbodies had detectable microcystin, only the fraction of samples that had measurable concentrations. For these ten studies we calculated the percent of samples with detectable concentrations. The collated data is available from Wilkinson and Shingai (2022).

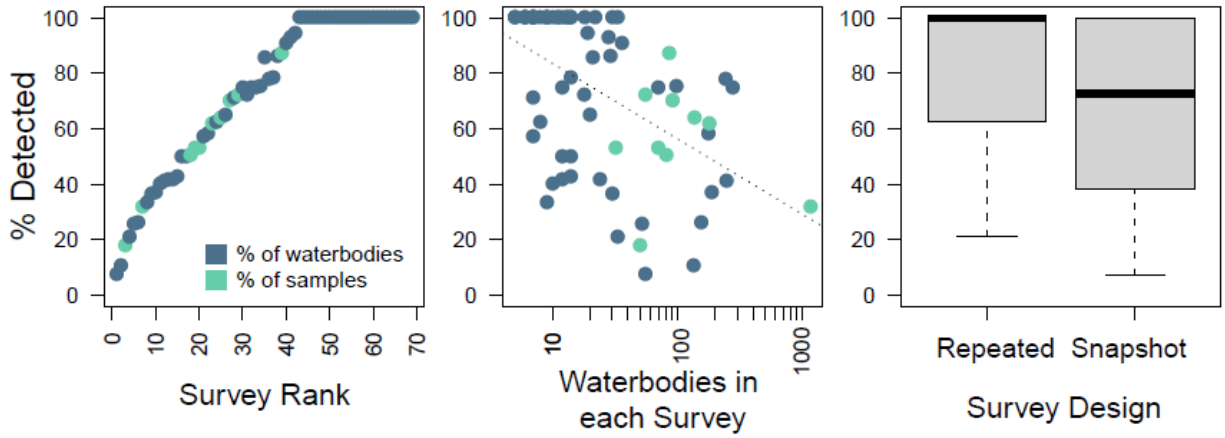

Figure 2. *The percent of waterbodies (blue) or water samples (teal) with a) detectable microcystin from 69 surveys ranked from lowest to highest percent detected among surveys, and b) the relationship between the number of waterbodies in each survey and the detection rate of microcystin in the water column (% detected = 111.06 – 27.4 × waterbodies in survey, p-value <0.001, R^2 = 0.27), and c) boxplots of the detection rate for repeated sampling surveys and snapshot (1-2 sampling events maximum) survey designs. There is a significantly higher detection rate among the population of repeated sampling surveys compared to the population of snapshot surveys reviewed in this study.*

Among all the surveys, the presence of a microcystin pool in the water column ranged from 7.3% to 100% of waterbodies or samples, with a median of 78% and mode of 100% (Figure 2a). This tallying exercise illustrates the ubiquity of microcystin in the water column of lakes and reservoirs. There was a significant negative correlation between the number of waterbodies or samples in a survey and the detection rate of microcystin (Figure 2b; F-value = 25.5, p-value <0.001, R^2 = 0.28). We hypothesized that this relationship was likely the result of survey design: surveys of many lakes are more likely to be spatially randomized with a single sampling event whereas surveys with a smaller number of lakes are more likely to be longitudinal with repeated sampling events on the same waterbodies. Based on the sampling designs reported, studies with repeated sampling designs had a significantly higher percent detection of microcystin in the water column than studies with a 'snapshot' design (Figure 2c; one-way ANOVA $F_{1,60}$ = 5.365, p-value = 0.024). Additionally, snapshot surveys had a significantly higher number of

waterbodies sampled compared to repeat sampling surveys (one-way ANOVA, $F_{1,60} = 6.03$, p-value = 0.017, number of waterbodies in each survey log-transformed). These findings support the hypothesis that the likelihood of microcystin being present in a waterbody sampled at one single point in time is lower than the likelihood of microcystin being present at any point over time in a waterbody sampled repeatedly.

Water Column Fluxes and Fates

The pool of microcystin in the water column has many potential fates (Figure 1). Two of the major fates for both intercellular and extracellular microcystin are degradation and transport into and out of the ecosystem through surface and groundwater flows, withdrawals for human use, and aerosolization. Additionally, microcystin can be lost or gained from the water column pool with connections to the sediment, macrophyte, and aquatic consumer pools, detailed in sections below.

Degradation Fluxes: Microcystin is removed from aquatic ecosystems through both photo- and biodegradation. Photodegradation rates are highest at ultraviolet wavelengths (Thirumavalavan et al. 2012) and lead to the rapid and efficient loss of extracellular microcystin from surface waters (Wörmer et al. 2010) (Table S2). This may be a particularly important mechanism in large shallow lakes with a high ratio of surface area to volume. The presence of humic substances may shield microcystin from photodegradation or act as a photosensitizer increasing degradation (Welker and Steinberg 2000). Biodegradation, performed by bacteria and fungi using hydrolytic enzymes to cleave the cyclic structure is another process that leads to substantial loss of microcystin from aquatic ecosystems (Dziga et al. 2013; Schmidt et al. 2014). Microbes that degrade cyanotoxins reside in both the water column and sediments and can even co-exist with cyanobacteria cells themselves (Dziga et al. 2013). Among ecosystems, the abundance of microcystin-degrading microbes is tightly coupled to microcystin availability, highlighting the important relationship between these two bacterial communities (Lezcano et al. 2018).

Based on rates reported in the literature, the average half-life of microcystin in the environment ranges from 0.5 – 22 days (Table S2). Many studies report a lag phase between the introduction of microcystin in the environment and peak degradation rates (Lezcano et al. 2018). Variation in the conditions that favor higher rates of biodegradation such as warm temperatures,

high pH, nutrient availability, and an oxic environment also contribute to the variation in rates among ecosystems and over time (Chen et al. 2010; Dziga et al. 2019). However, much of the information on microcystin biodegradation rates comes from studies performed in a water treatment setting. While advances have been made in isolating and identifying microcystin-degrading bacteria in waterbodies, additional data are needed to understand the seasonal dynamics and rates of biodegradation in aquatic ecosystems to adequately model the magnitude of this important flux at an ecosystem scale.

Transport Fluxes: In addition to endogenous production of microcystin, toxins produced outside of the ecosystem can be imported from upstream and exported from the ecosystem through hydrologic flows and human transport of water. The relative importance of surface hydrologic connections on microcystin import and export fluxes is likely higher in river networks with reservoirs (Graham et al. 2012; Ge et al. 2021) and marine coastal habitats connected to inland waters (Miller et al. 2010; Umehara et al. 2019). Microcystin can also be exported from a waterbody into the surrounding groundwater (Yang et al. 2016; Zhang et al. 2021) and be produced by cyanobacteria active in the vadose zone; however, it is unclear how sediment sorption dynamics might influence this flux (see below). Further research is needed to quantify the magnitude and seasonality of hydrologically driven import and export fluxes of microcystin from waterbodies. Human water export for drinking, irrigation, and transport (e.g., ballast water) can also alter the size of the water column microcystin pool.

Besides hydrologic and human transport, microcystin also leaves waterbodies and enters the atmosphere through the formation of spray aerosols. Wave action, mainly driven by wind, entrains air into the water resulting in the formation of bubbles that eject cyanobacteria cells and extracellular microcystin into the atmosphere upon bursting (Plaas and Paerl 2021). There is evidence that droplets are enriched in hydrophobic congeners of microcystin relative to the bulk concentration in the water (Olson et al. 2020). These droplets, commonly formed by wave action along the shoreline, can be inhaled by terrestrial organisms, including humans. The concentration of microcystin in spray aerosols from lakes ranges from 0.0018 to 50 ng m^{-3} (Table S3), based on the few measurements reported in the literature. Ultraviolet radiation and ozone can quickly degrade microcystin contained in aerosols (Jang et al. 2020). The residence time of microcystin-laden aerosols in the atmosphere, the distance traveled by aerosols, and the dynamic nature of cyanobacteria bloom and aerosol formation all influence the magnitude of this flux yet are

largely unresolved for freshwater ecosystems.

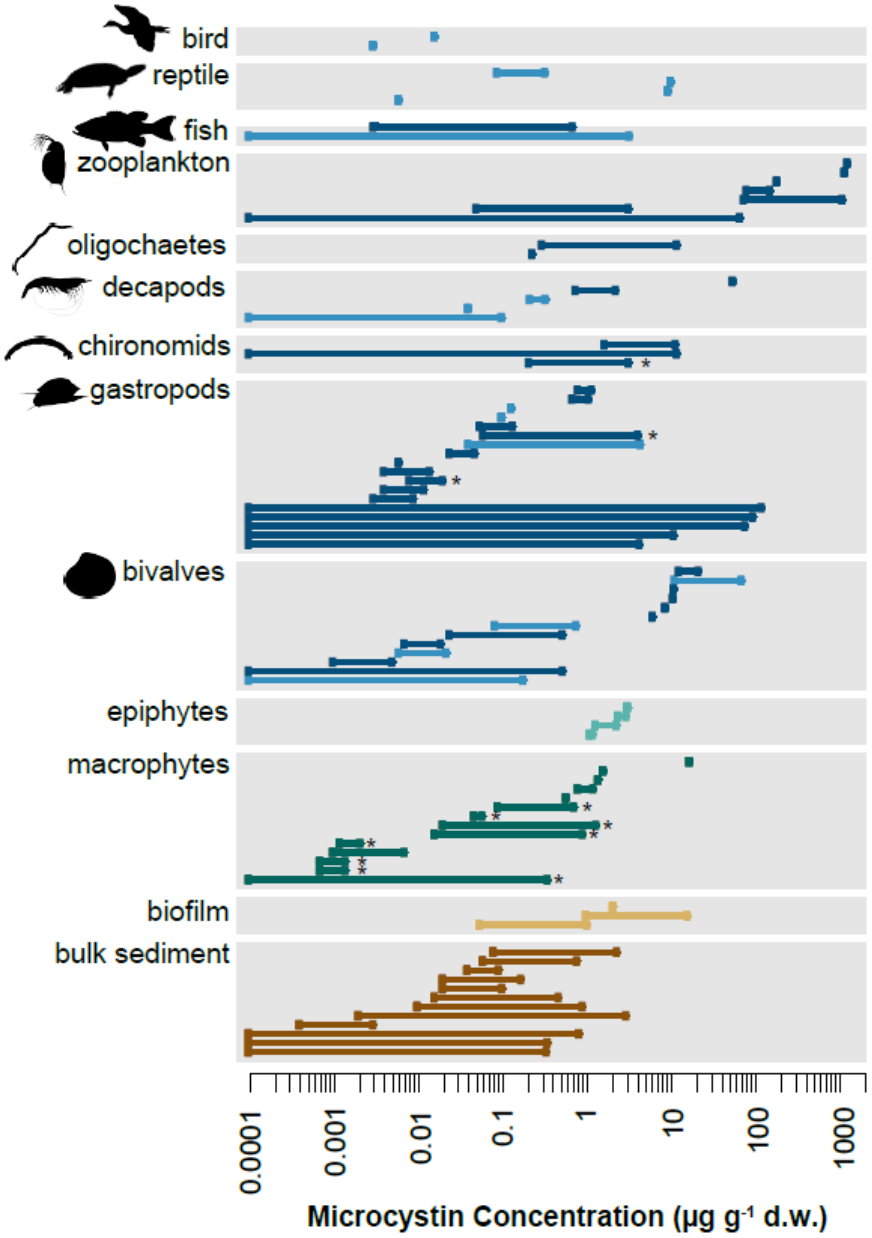

Figure 3. *The concentration of microcystin in various pools in comparable units (µg g^{-1} dry weight, d.w.; note the asterisk indicating the few measurements in µg g^{-1} wet weight, w.w.). Each line or point is a single study of concentration, with the line spanning the range of values reported in the study. For animals, light blue lines are microcystin concentrations in muscle tissue (common tissue for human consumption) and dark blue lines are concentrations in the whole body (consumption-based exposure through predation). Concentrations in other tissues (e.g., liver, hepatopancreas) are listed in Tables S6 and S7.*

B. **Sediment Pool**

Sub-Pools in Sediment

The bulk sediment pool of microcystin varies by orders of magnitude, from undetectable to 3 μg g^{-1} dry weight (d.w.) among lakes and over time (Figure 3, Table S4). The microcystin in the bulk sediment pool can be divided into microcystin bound in cells—either in biofilms, senesced, or dormant cells and colonies—dissolved in the pore water, and sorbed to sediment particles. The formation and persistence of microcystin-producing biofilms varies, but light-rich, shallow waters favor the development of cyanobacterial mats. The intercellular concentration of microcystin in biofilms ranges from 0.06 – 16 μg g^{-1} d.w. (Figure 3, Table S4).

In the dissolved form, microcystin can be found in the pore water between sediment particles. Microcystin can also adsorb to sediment particles, although there is a large range in maximum sorption capacity from 0.004 – 11.9 μg g^{-1} d.w. (Table S4) with some of the variation in sorption attributable to variation in congeners (Maghsoudi et al. 2015) and pH (de Maagd et al. 1999). In general, fine particles such as clay and sediments with high organic matter content have higher sorption capacity for microcystin (Munusamy et al. 2012).

Sediment Fluxes and Fates

As evidenced by the numerous sub-pools of microcystin in the sediments and the fluxes into, among, and out of these sub-pools (Figure 1), the sediments are an important component of the microcystin cycle. However, there have been few ecosystem-level investigations of sediment microcystin fluxes (Song et al. 2015), limiting our understanding of the role of this pool in ecosystem dynamics and human exposure risk, overall. One of the main fates of microcystin in the sediments is biodegradation. Biodegradation rates in the sediments are generally higher than the water column, with rates as high as 35 times faster in the sediments of some eutrophic ecosystems compared to the water column (Li et al. 2016).

The sedimentation of microcystin-containing cells and colonies contributes to the biofilm pool. Through resuspension and migration, approximately 0.8 – 3% of colonies reinvade the water column (Feng et al. 2019), moving microcystin from the sediment pool into the intercellular water column pool. The rate of microcystin resuspension and residence time in the water column is not well quantified but could be a cryptic pathway of human exposure when

water column production is otherwise low. Intracellular microcystin in the sediment pool is susceptible to movement into the extracellular pool through cell lysis or consumption and subsequent excretion by aquatic organisms (see "D. Aquatic Consumer Pool" section below). This dissolved pool in the sediments is subject to either diffusion back into the overlying water column, adsorption to sediment particles, or degradation by bacteria. In a rare comparison of rates within an ecosystem, Zastepa et al. (2017) found that the rate of microcystin diffusion from the sediments, at 1.38 ± 0.04 μg m^{-2} d^{-1}, was substantially higher than the burial rate, 0.13 ± 0.18 μg m^{-2} d^{-1}, in Lake of the Woods (North America), indicating that the sediments were a potential source of microcystin to the water column (Table S4).

C. Macrophyte Pool

Sub-Pools in Macrophytes

Macrophytes accumulate extracellular, dissolved microcystin into their roots, stems, leaves, flowers, seeds, and bulbs (Romero-Oliva et al. 2014) with concentrations up to 16.9 μg g^{-1} d.w. in some instances (Figure 3, Table S5). The allocation of microcystin among tissues within aquatic plants varies by species; however, the highest concentrations of microcystin are typically found in the roots and likely taken up from the sediment pool (Song et al. 2009). In addition to microcystin found within their tissues, macrophytes also provide the structural support for epiphytic cyanobacteria growth. While there is limited information regarding microcystin production by epiphytic cyanobacteria, reported concentrations vary from 1.16 – 3.12 μg g^{-1} d.w. of epiphyte biomass (Figure 3, Table S5).

Macrophyte Fluxes and Fates

The rate of microcystin uptake by macrophytes spans orders of magnitude (1.9 – 544 μg L^{-1} d^{-1}; Table S5), with much of the variability attributable to time since exposure, variation among species, and variation in uptake rates of microcystin congeners (Romero-Oliva et al. 2015). While the capacity for macrophytes to accumulate microcystin make them a potentially large sink of cyanotoxin in the environment, there is evidence that microcystin exposure can inhibit macrophyte growth by inducing physiological stress (Ujvárosi et al. 2019), potentially altering the strength of this sink. Once incorporated into the tissues of macrophytes, microcystin is removed from this pool through biotransformation and degradation (Table S5) (Pflugmacher

2004; Romero-Oliva et al. 2015), consumption of macrophyte tissues by organisms, release during plant decomposition, or incorporation into the sediment pool upon senescence.

D. Aquatic Consumer Pool

Sub-Pools of Aquatic Consumers

Aquatic consumer sub-pools include zooplankton, macroinvertebrates including shellfish and emergent insects, and vertebrates including fish that span trophic levels (Figure 3). Microcystin is incorporated into the tissues of aquatic organisms, particularly primary consumers (Papadimitriou et al. 2012), either through direct consumption of intercellular toxins, osmotic uptake of extracellular toxins, or consumption of lower trophic levels that have microcystin in their tissues. While direct toxicity to aquatic consumers is not usually widespread at lower microcystin concentrations, sub-lethal effects such as disruption of reproductive development (Zhang et al. 2019), increased sensitivity of juveniles (Gérard et al. 2005), and genotoxicity (Juhel et al. 2007) can all have population-level effects that influence ecosystem processes (Gérard et al. 2009).

Zooplankton are a key link in the aquatic food web between intercellular microcystin in the water column and higher trophic levels (Rohrlack et al. 1999). Primary consumers such as zooplankton mainly accumulate microcystin through direct consumption of cyanobacteria cells. Cladocera such as *Daphnia* graze on phytoplankton in the water column and ingest intracellular microcystin through filter feeding. Whole-body concentrations of microcystin are up to an order of magnitude higher in *Daphnia* compared to other aquatic invertebrates (Figure 3, Table S6) and can have adverse and sometimes lethal consequences for *Daphnia* (Rohrlack et al. 1999). Alternatively, microcystin exposure is hypothesized to provide medicinal protection against some parasites *Daphnia* (Sánchez et al. 2019).

In macroinvertebrates microcystin is introduced to tissues through consumption of cells and osmotic uptake of extracellular toxin through trans-tegument diffusion, oral water uptake, and gill or pulmonary breathing. While microcystin is detectable within whole-body tissues (Figure 3), the highest concentrations in macroinvertebrates are usually found in the hepatopancreas and intestines (Table S6). Species that feed by ingesting sediment accumulate larger amounts of extracellular microcystin that is sorbed to sediment particles (Lance et al. 2010). Non-selective feeders may have higher susceptibility to microcystin accumulation;

however, some macroinvertebrates have developed means for expelling, instead of ingesting, toxins (Juhel et al. 2006). Environmental and dietary exposure over longer periods of time can increase microcystin accumulation, however juveniles can have lower rates of accumulation, in part due to their less developed immune systems (Gérard et al. 2005).

Fish accumulate microcystin through epithelial uptake, direct consumption of phytoplankton, and bioaccumulation from prey (Zhang et al. 2009a; Flores et al. 2018). While studies of microcystin accumulation in fish most commonly evaluate concentrations in liver and muscle tissues (Figure 3), a recent meta-analysis of fish tissues revealed that the toxin is also found in the blood, heart, reproductive organs, gut, gills, and skin of fishes (Flores et al. 2018) (Table S7). The highest reported concentration of microcystin contained within fish tissues was 375.3 $\mu g\ g^{-1}$ d.w. in the liver of planktivorous smelt (Flores et al. 2018). Microcystin accumulation in fish varies by species and location but is positively correlated with microcystin concentrations in the surrounding water column (Poste et al. 2011; Flores et al. 2018). Feeding strategy also influences microcystin accumulation with higher concentrations in omnivorous fish compared to planktivorous and piscivorous fishes.

Aquatic Consumer Fluxes and Fates

Microcystin bioaccumulation is consistently observed in zooplankton, planktivorous fishes, and bivalves (Kozlowsky-Suzuki et al. 2012; Gibble et al. 2016). The rate of microcystin accumulation in aquatic consumers depends on animal behavior and environmental factors. For example, in zooplankton accumulation rates vary depending on environmental effects on filter feeding rates (e.g., temperature) as well as population-level adaptations to cyanotoxins such as avoidance of ingesting intercellular microcystin following exposure to the toxin (Tillmanns et al. 2011; Wojtal-Frankiewicz et al. 2013). Population-level effects of microcystin accumulation on fitness are also possible if the toxin accumulates in the reproductive tissues with the potential to be passed on to future (Zhang et al. 2007).

Predation is another flux of microcystin between aquatic consumers that leads to bioaccumulation, however there is limited evidence that microcystin biomagnifies in the food chain (Papadimitriou et al. 2012; Kozlowsky-Suzuki et al. 2012). In some food chains there is evidence of microcystin biodilution (decreasing concentration with increasing trophic level), but this does not appear to be common. The potential flux of microcystin from prey to predator is

dependent on the tissues consumed. Toxins are often concentrated in digestive organs such as the stomach, intestines, liver or hepatopancreas (see Tables S6-S7). As such, consumption of the whole organism will likely result in higher microcystin exposure than consumption of muscle tissue alone (e.g., humans consuming fish fillets).

Once consumed or absorbed and incorporated into organismal tissues, microcystin is excreted, egested, or undergoes biotransformation (i.e., depuration), resulting in detoxification (Schmidt et al. 2014). Biotransformation resulting in detoxification has been documented in *Daphnia* tissues (Wojtal-Frankiewicz et al. 2013), in the digestive glands of macroinvertebrates (Schmidt et al. 2014), and in fish (Flores et al. 2018). Excretion is another flux from aquatic consumers to other pools including the water column and sediment. While microcystin excretion has been documented in fish and other organisms, the sedimentation of fecal pellets and concentration of toxins is not well quantified.

E. Terrestrial Environment

Sub-Pools in the Terrestrial Environment

Microcystin has been found in the tissues of many terrestrial animals, with the highest concentrations in aquatic-associated wildlife including waterfowl, turtles, and reptiles (Figure 3; Table S7). Microcystin can also accumulate in crops via contaminated irrigation water. An assay experiment to investigate bioaccumulation of microcystin in lettuce (*Lactuca sativa L.*) revealed that toxin the accumulated in the foliar tissues of the plants regardless of the concentration in the irrigation water (Romero-Oliva et al. 2014). There is also evidence that microcystin can accumulate in soils (Zhang et al. 2021). In livestock, microcystin can accumulate through watering from a microcystin-contaminated source and potentially be passed to other terrestrial consumers.

Terrestrial Fluxes and Fates

Microcystin found in terrestrial environments mainly originates from the water column and aquatic consumer pools. Originating from the water column, microcystin aerosol concentrations vary widely with bloom and wind conditions, but this is generally a diffuse flux. Microcystin-laden water withdrawn for drinking or irrigation purposes introduces the toxin to terrestrial consumers (i.e., wildlife, livestock, humans) and soils (Zhang et al. 2021). Animal

movement between the aquatic and terrestrial environment (e.g., insect emergence and human recreation) as well as predation are another flux between these spheres (Moy et al. 2016). Of particular concern are the fluxes of microcystin that create cryptic pathways of human exposure.

Humans are exposed to microcystin through many pathways, including oral ingestion during recreation or from drinking water, consuming contaminated foods and supplements, dermal contact, and inhalation of aerosols (Carmichael and Boyer 2016). However, the predominant pathway of microcystin exposure to humans is ingestion of contaminated drinking water or ingestion during recreation (Giannuzzi et al. 2011). Communities that rely on untreated drinking water from lakes, reservoirs, and groundwater wells with microcystin concentrations that exceed recommended thresholds for ingestion are particularly vulnerable (Zhang et al. 2009b; Ruibal-Conti et al. 2019). Additionally, when microcystin makes its way into domestic water supplies, hygienic activities such as bathing and hand washing become a pathway of exposure through respirable water particles (Benson et al. 2005).

Microcystin in animal tissues that humans consume is another cryptic pathway of exposure. In general, tissue concentrations in fish and shellfish are high when the surrounding water column concentrations are high (Ibelings and Chorus 2007; Poste et al. 2011; Flores et al. 2018). When microcystin concentrations are high in the water column, consumption of whole animals such as bivalves can result in 8-23.5 times the tolerable daily load for humans as defined by the World Health Organization (Chen and Xie 2005). Preparation method can also affect exposure risk, as boiling animal muscle tissue (e.g., fish fillets) has been shown to release microcystin otherwise bound to phosphate (Berry et al. 2011).

Comparing Magnitudes of Pools and Fluxes

Quantitative Comparison

Through the literature synthesis we identified studies of pools and fluxes from a diversity of inland waters employing a variety of measurement methods and reported units. While it is not feasible to construct a full quantitative cycle using the literature synthesis, we can further synthesize the reported values to compare the magnitude of pools and fluxes and identify poorly parameterized processes. To do this, we used a subset of studies that reported pools and fluxes in consistent and comparable units. For each of these studies, we extracted or calculated mean and standard deviations for pool and flux values reported. For studies without a reported variance, we

estimated the standard deviation using the linear relationship between mean and standard deviation (s.d.) for all pools and fluxes (s.d. = -1.35 × 0.99 × mean; $F_{1,61}$=327.9, p-value <0.001, R^2 = 0.84). The population of means and standard deviations collected from the literature for a given pool or flux were used in a random effects model with a restricted maximum likelihood estimator method to estimate the mean pool or flux magnitude and 95% confidence intervals (CI) (Figure 4). This analysis was performed using the *metafor* package in R version 4.1.3 (Viechtbauer 2010).

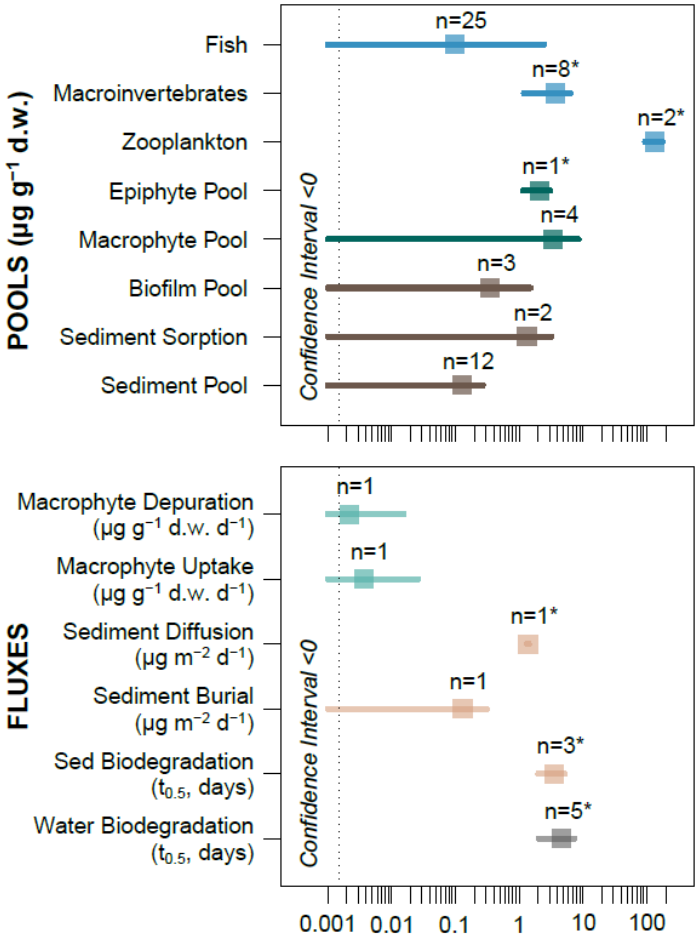

Figure 4. *The estimate of the mean magnitude (square) and 95% confidence interval (line) of various pools (top panel) and fluxes (bottom panel) in a random effects model using a subset of studies from the literature with comparable units of measurement. A log scale was used for visualization, and therefore confidence intervals that included zero were set to 0.001 for plotting and the confidence interval crosses the vertical dashed line denoting zero. Mean estimates with a 95% confidence interval not including zero have an asterisk next to the bar. The number of studies (n) contributing to each estimate is displayed above each estimate.*

In general, there were few studies with comparable units for estimating the magnitude of pools and fluxes and high variance within and among studies (Figure 4). Only six of the fourteen mean estimates had confidence intervals that did not include zero. Despite this high degree of uncertainty and variation in measurement methods, some patterns did emerge that can be cautiously interpreted. The mean concentration of microcystin in sediments (0.13 µg g^{-1} d.w, [-

506 0.01, 0.27 CI]) was an order of magnitude lower than the mean sediment sorption capacity (1.3
507 μg g^{-1} d.w, [-0.57, 3.27 CI]), potentially indicating that fluxes resulting in loss of microcystin
508 from the sediment pool (e.g., burial, diffusion) can actively reduce concentrations below sorption
509 capacity. However, the estimates for both pools had confidence intervals that included zero. The
510 mean half-life for sediment biodegradation (3.57 days [2.01, 5.13 CI]) was similar to the half-life
511 in the water column (4.67 days [2.028, 7.32 CI]) in this among-study comparison. The mean
512 concentrations in macrophyte tissue (3.45 μg g^{-1} d.w, [-1.58, 8.49 CI]), the epiphyte pool (2.10
513 μg g^{-1} d.w, [1.15, 3.05 CI]), and the sediment biofilm pool (0.35 μg g^{-1} d.w, [-0.81, 1.51 CI])
514 indicate the magnitude of the primary producer reservoir of microcystin not found in the water
515 column pool. For aquatic consumers, the mean zooplankton concentration was the highest of any
516 pool (134.7 μg g^{-1} d.w, [94.5, 175.1 CI]), followed by macroinvertebrates (values only available
517 for oligochaetes, bivalves, a gastropod, and chironomid; 3.75 μg g^{-1} d.w, [1.19, 6.32 CI]). The
518 estimate for whole fish was taken from another meta-analysis that was based on 25
519 measurements (Flores et al. 2018).
520
521 ***Consideration of Temporal Dynamics***
522 When cyanobacteria bloom—by definition, an episodic event—the pool of microcystin in
523 the water column and/or biofilm can increase during this period. Given the detrimental effects of
524 microcystin to human health, a great deal of research effort has focused on understanding the
525 temporal dynamics of blooms and toxin production (Rastogi et al. 2015), even during periods of
526 ice cover (Wejnerowski et al. 2018). The seasonality of blooms and toxin production likely also
527 produces strong temporal dynamics in the other pools (e.g., animal and macrophyte tissues) and
528 fluxes (e.g., sedimentation, biodegradation) of microcystin, particularly when coupled with
529 variable turnover times in aquatic ecosystems.
530 Turnover times span many orders of magnitude, from a few minutes for a limiting
531 reactant like microcystin for a biodegrading bacterium to months for animal tissues to years for
532 sediment pools. This mismatch in turnover times allows legacies of past events to shape current
533 ecosystem dynamics (Carpenter and Turner 2000). For organisms, tissue turnover time,
534 microcystin accumulation rates, and toxin metabolism (Schmidt et al. 2014) combine with the
535 availability of microcystin from other pools to dictate storage and persistence of the toxin in the
536 aquatic food web. Organisms in lakes where blooms only occur seasonally may pose less of a

threat to humans consuming them depending on the time since the bloom and opportunity for depuration and tissue turnover. On the other hand, the long tissue turnover times of some organisms such as bivalves and fish muscle (Vander Zanden et al. 2015) may result in a "hidden" pathway of human exposure when consumed weeks after a toxic bloom has subsided. Similarly, bloom seasonality in combination with plant phenology and tissue turnover may also affect microcystin accumulation in crops that are irrigated with microcystin-laden water supplies (Romero-Oliva et al. 2014).

Future Directions and Research Needs

Constructing a comprehensive biogeochemical microcystin cycle revealed gaps in our understanding of ecosystem-scale microcystin dynamics. Despite the pools and fluxes identified from the literature synthesis, many unknowns remain pertaining to specific mechanisms and environmental factors that favor the movement and accumulation of microcystin within and among the pools. Future investigations of microcystin movement and accumulation in aquatic environments should focus particularly on fluxes to and from the sediment, environmental drivers of biodegradation, and the seasonal dynamics of the aquatic food web pool.

Sediments are an active pool of microcystin in freshwater environments (Figure 4) (Zastepa et al. 2015). However, the current handful of ecosystem-level investigations of sediment microcystin fluxes limits our understanding of the magnitude and role sediments play in microcystin dynamics overall. For example, there is evidence indicating microcystin resuspension from sediments is a potential source of microcystin into the water column (Maghsoudi et al. 2015), but it is unclear when, where, and how much this flux contributes to the water column pool. Incorporating sediment-water exchange of microcystin into models and applying these to ecosystem level investigations would generate valuable insight into the role of sediments in microcystin movement and accumulation.

Similarly, there is currently little information on the seasonal dynamics and environmental drivers of microcystin biodegradation in both the water column and sediments. While advances have been made in isolating and identifying microcystin-degrading bacteria, additional data are needed to understand the seasonal dynamics and mechanisms that control rates of biodegradation at an ecosystem scale. Accurately quantifying this important loss term in

567 the microcystin cycle will require scaling bottle experiments from a controlled laboratory setting
568 to the whole ecosystem scale which is heterogenous in both space and time.
569 While there are observational studies of microcystin dynamics in consumers in natural
570 environments, much of the information we have regarding microcystin accumulation in aquatic
571 organisms comes from toxicology-type studies with exposure treatments performed in a
572 laboratory setting. Additional study of the duration and magnitude of microcystin accumulation
573 in organism tissues seasonally and long-term would provide valuable insight into the dynamics
574 of the aquatic consumer pool following bloom events. Another avenue of microcystin movement
575 that remains poorly understood are the predominant uptake pathways in aquatic organisms and
576 the role of environmental regulation of these rates. Similarly, the rates of microcystin excretion
577 and egestion are poorly quantified. Further investigations of microcystin fluxes across aquatic-
578 terrestrial interfaces and along the aquatic continuum (i.e., from inland to coastal ecosystems) are
579 also needed to better capture the exogenous inputs available for consumer uptake. For example,
580 limited information exists on microcystin flux via emergent aquatic insects from the aquatic to
581 terrestrial environment (Moy et al. 2016). Similarly, the hydrologic fluxes of microcystin
582 downstream into the marine environment poses a threat to wildlife (Miller et al. 2010) and
583 humans consuming contaminated shellfish (Gibble et al. 2016).
584 Finally, the development of full microcystin budgets for watersheds requires investigators
585 across various fields to report values in a 'common currency' that can be incorporated into
586 ecosystem models. For example, measurements of pools need to be in mass per unit area or
587 volume and fluxes in mass per unit area or volume per unit time. While we were able to compare
588 some microcystin pools across the literature ($\mu g\ g^{-1}$ d.w.; Figure 3 and 4), measurements reported
589 in this common currency were lacking for some important pools, preventing us from developing
590 a full, quantitative budget.
591
592 **Conclusions**
593 The conceptual biogeochemical model for microcystin that we constructed identified the
594 major pools and fluxes of this toxin for inland waterbodies. From the quantitative synthesis we
595 presented (Figure 4) it is evident that microcystin is present and moves through many
596 components of the ecosystem besides the water column. Given the many fluxes into and out of
597 the water column (e.g., import from upstream, sediment diffusion), the visual presence of bloom

598 is not necessarily indicative of exposure risk for humans. This conceptual model can be used as
599 the framework for developing ecosystem mass balances of microcystin to quantify the transport
600 and transformation of this toxin both in freshwater and marine ecosystems. Adopting the
601 framework of a "microcystin cycle" will not only improve our understanding of processes
602 driving toxin prevalence but will also help to prioritize effective strategies for the management of
603 microcystin exposure risks to humans and wildlife.
604
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614 (reptile), Gabriela Palomo-Munoz (bird; CC BY-NC 3.0).

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848

Supplementary Material

Microcystin as a biogeochemical cycle:
pools, fluxes, and fates of the cyanotoxin in aquatic ecosystems

Quin Shingai and Grace M. Wilkinson

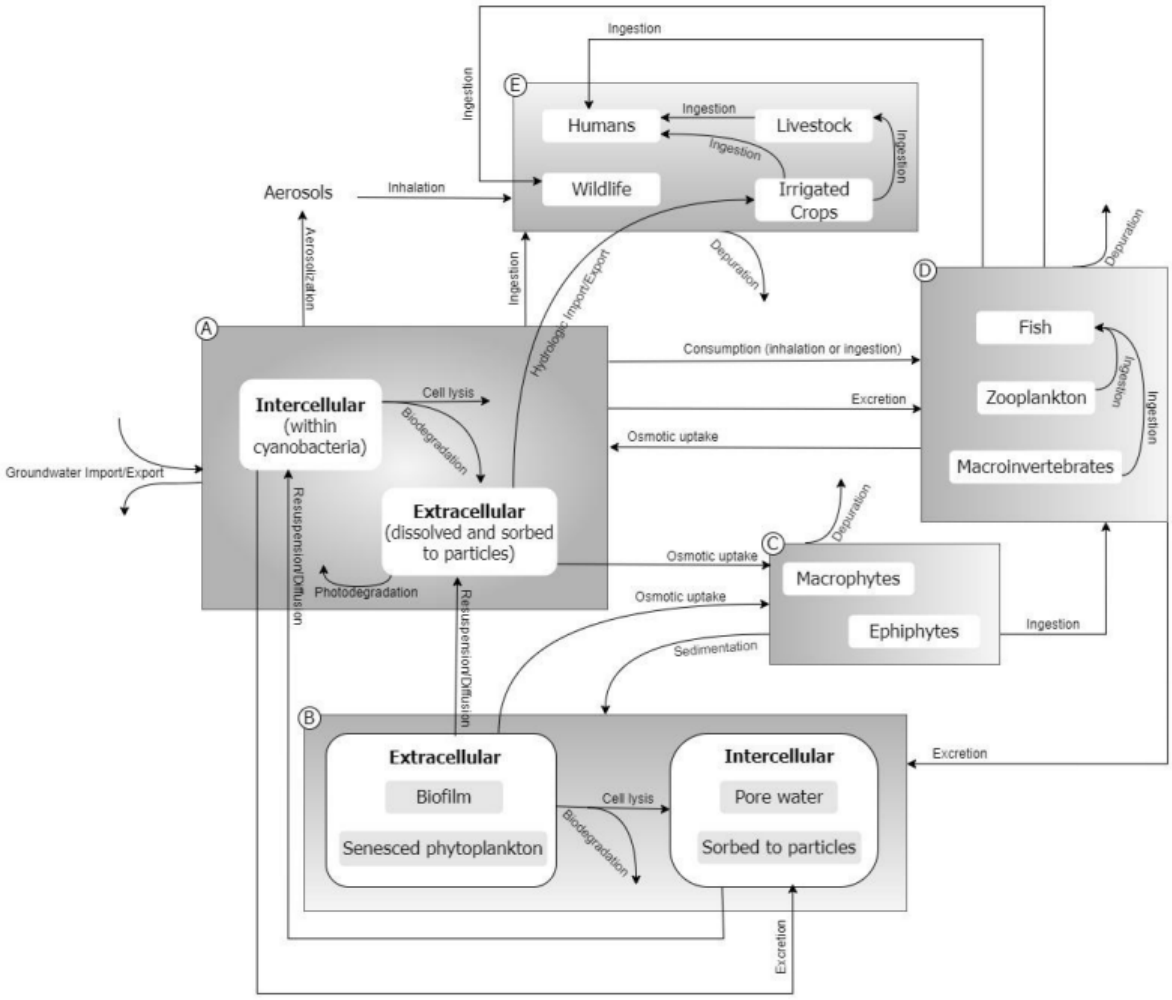

Figure S1. A simplified box and arrow diagram of the conceptual microcystin cycle presented in Figure 1 in the main text. The major pools (A-E) of microcystin and sub-pools are labeled in the diagram in light grey boxes. The fluxes are denoted with arrows and labeled. The fluxes (arrows) are between the major pools and inclusive of all sub-pools unless arrows specifically connect two sub-pools.

Supplementary Tables

Table S1. Studies that contain surveys of microcystin concentrations in the water column (data underpinning Figure 2 in main text).

Citation	# waterbodies sampled	# samples	# waterbodies (or samples) with microcystin detected	% detection	Notes
(Lindholm et al. 2003)	55		4	7.3	Survey conducted in 1999
	134		14	10.4	Survey conducted in 2000
(Hirooka et al. 1999)	50	50	9 samples	18.0	
(Cook et al. 2004)	33		7	21.2	
(Howard et al. 2017)	52		13	25.4	depressional wetland sites, detection from all three years combined
(Frank 2002)	155		40	26.0	
(Loftin et al. 2016)	1161	1252	400 samples	32.0	only reported detections based on samples, but most lakes sampled once; note that (Beaver et al. 2014) only reported detections above 1 μg L^{-1} for the same survey
(Kaggwa et al. 2018)	9		3	33.3	
(Mohamed and Al Shehri 2007)	30		11	36.7	30 reservoirs, 15 covered (no detects) and 15 open reservoirs
(Bigham et al. 2009)	187		69	36.9	Based on information provided in Table 2
(Zagajewski et al. 2009)	10		4	40.0	
(Orihel et al. 2012)	246		101	41.0	exceeded WHO guideline of >1 ug/L, not total detection
(Mrdjen et al. 2018)	24		10	41.7	from supplemental info table
(Okello et al. 2009)	12		5	41.7	Includes 3 sites in Lake Victoria from geographically separated bays
(Kotak et al. 1993)	14		6	42.9	
(Balode et al. 2006)	14		7	50.0	Sampled over many years, usually monthly
(Pavlova et al. 2006)	12		6	50.0	12 lakes investigated, 6 lakes sampled, 8 samples from those lakes all had detectable microcystin concentrations
(Boyer 2007)	81	2286	1155 samples	50.5	
(Turner et al. 2018)	70	137	72 samples	53.0	only reported based on the number of samples above 0.2 ug/L

(Willame et al. 2005)	32	32	17 samples	53.1	Despite surveying 250 lakes and sampling 49, only quantified microcystin concentration in 32 waterbodies
(Carrasco et al. 2006)	7		4	57.1	
(Graham and Jones 2009)	177		103	58.2	
(Kotak and Zurawell 2007)	180	900	558 samples	62.0	
(Menezes et al. 2017)	8		5	62.5	Based on hundreds of samples collected from 2000-2015
(Hayes and Vanni 2018)	136	195	125 samples	64.1	
(Barros et al. 2019)	20		13	65.0	samples taken over multiple years
(Bláhová et al. 2007)	91	206	145 samples	70.4	
(Bittencourt-Oliveira et al. 2012)	7		5	71.4	7 reservoirs sampled 27 times, 5 reservoirs had quantifiable MC using HPLC
(Fastner et al. 1999)	55	533	385 samples	72.0	
(Heiskary et al. 2014)	277		209	75.0	
(Koker et al. 2017)	18		13	72.2	
(Bláhová et al. 2008)	70		53	75.0	
(Park et al. 1998)	12		9	75.0	based on information presented in Table 2
(Kobos et al. 2013)	98		74	75.5	from table of literature synthesis, not new data in this study
	21		18	85.7	Only the new data presented in this study
(Graham et al. 2004)	241		188	78.0	
(Christophoridis et al. 2018)	14		11	78.6	based on information presented in Table 1
(Vezie et al. 1997)	29		25	86.2	
(Faassen and Lürling 2013)	86	88	77 samples	87.5	used 88 samples because no indication which lakes were sampled twice
(Gkelis et al. 2015)	36		33	91.0	
(Messineo et al. 2009)	28		26	92.9	based on the data in figures 2-3
(Jančula et al. 2014)	19		18	94.7	
(Beversdorf et al. 2017)	6		6	100.0	
(Bukowska et al. 2017)	7		7	100.0	
(Carrasco et al. 2006)	7		7	100.0	in 2003 all 7 reservoirs had detectable MC
(Gkelis et al. 2005)	7		7	100.0	sampled blooms only, found MC in all samples

(Jacoby et al. 2015)	9	9	100.0	MC detected at least once in each lake
(Kemp and John 2006)	13	13	100.0	wetlands
(Lorenzi et al. 2018)	11	11	100.0	
(Mohamed et al. 2016)	6	36	100.0	
(Okello et al. 2010)	5	5	100.0	
(Prakash et al. 2009)	5	5	100.0	
(Trout-Haney et al. 2016)	18	18	100.0	
(Boutte et al. 2008)	11	11	100.0	
(Cerasino and Salmaso 2012)	9	9	100.0	data from Table 3
(Farkas et al. 2014)	14	14	100.0	
(Fromme et al. 2000)			100.0	did not report the number of samples or lakes, just that there was 100% detection
(Giani et al. 2005)	22	22	100.0	
(Gkelis and Zaoutsos 2014)	6	6	100.0	
(Haddix et al. 2007)	33	33	100.0	biweekly sampling of raw water sources
(Kotak 2000)	13	13	100.0	
(Lindon and Heiskary 2009)	12	12	100.0	
(Mankiewicz et al. 2005)	7	7	100.0	
(Mazur-Marzec et al. 2008)	7	7	100.0	
(Mooney et al. 2011)	14	14	100.0	
(Poste et al. 2013)	8	8	100.0	
(Sinang et al. 2015)	10	10	100.0	
(Vasconcelos et al. 1996)	9	9	100.0	collected/targeted bloom samples
(Wu et al. 2015)	30	30	100.0	

Table S2. Sediment and water column microcystin degradation rates.

Pool or Flux	Waterbody	Habitat	Rate or t_{50}	Citation
Biodegradation rate of natural microbial assemblages	Lake Taihu, China	water	49.21 μg L^{-1} d^{-1}	(Li et al. 2016)
		sediment	1727 μg L^{-1} d^{-1}	
	Svratka River, Czech Republic	river water	$t_{1/2}$ = 8 days	(Babica et al. 2005)
		biofilm	$t_{1/2}$ = 0.83 days	
	Lake Taihu, China	water	$t_{1/2}$ = 0.85 – 16.23 days	(Chen et al. 2008)
		sediment	$t_{1/2}$ = 0.83 – 1.19 days	
	Lake Dianchi, China	Sediment, anoxic conditions	$t_{1/2}$ = 3.86 days	(Chen et al. 2010)
		sediment, oxic conditions	$t_{1/2}$ = 2.68 days	
	Lake Taihu, China	sediment, anoxic	$t_{1/2}$ = 3.26 – 4.70 days	(Wu et al. 2015)
	Lake Erhai, China	sediment, anoxic	$t_{1/2}$ = 4.70 – 7.07 days	
	Lake Xingyun, China	sediment, anoxic	$t_{1/2}$ = 4.33 days	
	Lake Fuxian, China	sediment, anoxic	$t_{1/2}$ = 5.48 days	
	Lake Dianchi, China	sediment, anoxic	$t_{1/2}$ = 2.55 – 6.38 days	
	Grafham Water, England	water	$t_{1/2}$ = 3-4 days	(Cousins et al. 1996)
	lake in Ontario, Canada	dissolved fraction in water	$t_{1/2}$ = 1.5 – 8.5 days	(Zastepa et al. 2014)
	Lake Yangebup, Australia	sediment	$t_{1/2}$ = 0.54 – 0.92 days	(Song et al. 2014)
	Lake Burragorang, Australia	Water	$t_{1/2}$ = 0 – 22.2 days	(Ho et al. 2012)
	Sandy aquifer material	aquifer material, aerobic conditions	λ = 1.87 d^{-1}	(Grützmacher et al. 2010)
		aquifer material, anaerobic conditions	λ = <0.01 – 1.35 d^{-1}	
Photodegradation Rate	Valmayor Reservoir	water column	78.7% lost in 22 days	(Wörmer et al. 2010)
	Taiwan Reservoirs and Rivers	water column	1.6 μg L^{-1} hr^{-1}	(Munusamy et al. 2012)

**$t_{1/2}$ = the time until 50% of initial amount of microcystin was degraded*

λ = decay constant

Table S3. Rates of import, export, and aerosolization.

Pool or Flux	Waterbody	Concentration or Rate	Notes	Citation
Aerosol Concentration	Lakes in northeastern USA	<13 – 384 pg MC m^{-3}	Concentrations not specified to sampled lake	(Murby and Haney 2016)
	Lakes Forsyth and Rotura, New Zealand	1.8 pg MC m^{-3}	Low and high volume air samplers deployed	(Wood and Dietrich 2011)
	Bear Lake, MI (USA)	0 – 80 pg MC m^{-3}	Personal air samplers worn by lake recreators	(Cheng 2007)
	Mona Lake, MI (USA)	50,000 ± 20,000 pg MC m^{-3}	Aerosol particles generated in the lab from lake water samples	(Olson et al. 2020)
	Two reservoirs in California (USA)	<0.1 – 2,890 pg MC m^{-3}	Personal air samplers	(Backer et al. 2010)
		0.6 ± 0.8 ng	Nasal swabs of recreators on the lake	
	Lake in Michigan	7,702 ± 13,248 pg MC m^{-3}	High volume sampler at shoreline	(Backer et al. 2008)
	Nasal swabs for mucus concentration of MC	0.65 ± 0.71 ppb	115 nasal swabs from humans	(Schaefer et al. 2020)
Aerosol Degradation	NA	54 minutes	Estimate of lifetime of microcystin in aerosols	(Jang et al. 2020)
Import/Export	Lake Chaohu groundwater	0.17 – 1.07 μg L^{-1}	Samples from 15 wells	(Yang et al. 2016)

Table S4. Sediment concentrations of microcystin or flux rates from the sediments.

Pool or Flux	Waterbody & Location	Rate or Concentration	Notes	Citation
Intercellular Concentration in Biofilms	Ojós Reservoir, Spain	0.56 ± 0.17 (s.e) μg L^{-1}	Intracellular concentrations, range was 0.08 – 2.11 μg L^{-1} for 11 samples	(Hurtado et al. 2008)
	Villerest Reservoir, France	0.021 ± 0.14 pg $cell^{-1}$	Concentration in initial sediment samples prior to experiments	(Misson et al. 2011)
	Lake Grangent, France	0.058 – 0.442 pg $cell^{-1}$	Only sampled surface sediment layers representing 2003 - 2008	(Misson et al. 2012)
	Lake Mokoan, Australia	0.002 μg g^{-1} d.w.	In dried, cyanobacterial crust along the lakeshore	(Jones et al. 1995)
	Myall Lakes, Australia	1.4 – 2.5 μg L^{-1}	Shallow lake with now nutrient concentrations	(Dasey et al. 2005)
	Antarctica	1 – 16 μg g^{-1} d.w.	Cyanobacterial mats from various ponds, lakes, and hydroterrestrial environments in the Dry Valleys and Bratina Island	(Wood et al. 2008)
	Lake Caohai, China	0.008 – 0.06 pg $cell^{-1}$	Range of values across several experimental treatments	(Feng et al. 2019)
	Alharabe River, Spain	20.45 mg m^{-2}	Total benthic community production	(Aboal et al. 2005)
	Segura basin reservoirs, Spain	0.055 – 1.032 μg g^{-1} d.w.	Intercellular microcystins	(Asencio 2013)
	Alpine lakes, Switzerland	0.0 – 12.2 μg g^{-1} MC-LR per unit protein	Biofilm measurements over two years in five high elevation lakes	(Mez et al. 1997)
Recruitment of Colonies from Sediments	Lake Caohai, China	0.78 – 2.8% of benthic cells present	Undamaged benthic *Microcystis*, undisturbed & disturbed conditions	(Feng et al. 2019)
		0.08 – 0.28% of benthic cells present	Damaged benthic *Microcystis*, undisturbed & disturbed conditions	
	Villerest Reservoir, France	0.47% ± 0.10 of colonies per day	Estimates from control media only	(Misson et al. 2011)
	Quitzdorf Reservoir, Germany	3% of benthic colonies	Ecosystem level estimate during "reinvasion" phase/season	(Ihle et al. 2005)
Bulk Sediment Concentration	Lake Yangebup, Australia	0.06 – 0.78 μg g^{-1} d.w.	Shallow, eutrophic lake	(Song et al. 2015)
	Lake Głębokie, Poland	0.01 – 0.91 μg g^{-1} d.w.	Shallow, eutrophic lakes	(Pawlik-Skowrońska et al. 2010)
	Lake Syczyńskie, Poland	0 – 0.34 μg g^{-1} d.w.		
	Lake Taihu	0.02 – 0.17 μg g^{-1} d.w.	Range in surface sediments from four sampling locations	(Chen et al. 2008)
	Various lakes in Canada	n.d. – 0.83 μg g^{-1} d.w.	Range of values detected over various sediment intervals in seven lakes	(Zastepa et al. 2015)

	Lake of the Woods	0.15 ± 0.20 μg g^{-1} d.w.	Sum of congeners, mean value from three sites in lake	(Zastepa et al. 2017a)
	Lake Baptise, Canada	0.002 – 3 μg g^{-1} d.w.	Concentrations over core profile, highest concentration at the surface	(Zastepa et al. 2017b)
	Lake Tsukui	0.08 – 2.33 μg g^{-1} d.w.	From samples throughout the sediment profile	(Tsuji et al. 2001)
	Nile River	0.039 – 0.092 μg g^{-1} d.w.	Encompasses range of concentrations measured in the river and irrigation canals	(Mohamed et al. 2007)
	Lake Amatitlàn, Guatemala	0.02 – 0.101 μg g^{-1} organic matter	Range of concentrations within sediment core going back >2000 years	(Waters et al. 2021)
	Lake Griffin, Florida USA	0.0004 – 0.003 μg g^{-1} organic matter	Range of concentrations within sediment core going back >4000 years	(Waters 2016)
	Brno Reservoir, Czech Republic	0.016 – 0.474 μg g^{-1} d.w.	34 sediment samples analyzed by HPLC	(Babica et al. 2006)
Sedimentation Rate	Various reservoirs in Spain	0.1 – 0.8 m d^{-1}	Settling rate for individual colonies of *Microcystis*	(Cirés et al. 2013)
	Isahaya Bay Reservoir, Japan	0.83 mg m^{-2} d^{-1}	From ecosystem-scale estimate of 21.5 kg d^{-1} for 2600 ha reservoir	(Umehara et al. 2019)
	Various reservoirs in Spain	0.01 – 2.53 mg m^{-2} d^{-1}	Values for microcystin-containing particles, not microcystin content alone	(Wörmer et al. 2011)
Burial Rate	Lake of the Woods, Canada	0.13 ± 0.18 μg m^{-2} d^{-1}	Sum of congeners, mean value from three sites in lake	(Zastepa et al. 2017a)
	Dewey Lake, Nebraska USA	0.0002 – 0.0240 μg cm^{-2} y^{-1}	Range of value across a sediment core	(Efting et al. 2011)
Diffusion Rate	Lake of the Woods, Canada	1.38 ± 0.04 μg m^{-2} d^{-1}	Sum of congeners, mean value from three sites in lake	(Zastepa et al. 2017a)
Sediment Pore Water Concentration	Various lakes in Canada	n.d. – 0.13 μg L^{-1}	Range of values detected over various sediment intervals in seven lakes	(Zastepa et al. 2015)
	Lake of the Woods	3.21± 0.50 μg L^{-1}	Sum of congeners, mean value from three sites in lake	(Zastepa et al. 2017a)
Maximum Sediment Absorption Capacity	Emerald and Jade Reservoirs, Taiwan	6 – 11.9 μg g^{-1} d.w.	Sediments spiked with MC-LR solution and absorption measured	(Munusamy et al. 2012)
	Various river sediments, Taiwan	1.44 – 2.32 μg g^{-1} d.w.		
	Lake Champlain, Canada	0.004 – 0.041 μg g^{-1} d.w.	Natural sediment experiments	(Maghsoudi et al. 2015)
	Various lakes in Finland	13 – 24 μg mL^{-1} sediment	Based on sterilized sediment treatments	(Rapala et al. 1994)

Table S5. Microcystin concentrations in macrophyte tissues and uptake rates.

Pool or Flux	Species	Tissue	Concentration	Notes	Citation
Macrophyte Tissue Concentration	*Ceratophyllum submersum*	whole plant	1.01 ± 0.21 μg g^{-1} d.w.		(Ujvárosi et al. 2019)
	Lemna minor	whole plant	0.09 – 0.72 μg g^{-1} f.w.	Range of values from exposure to 0.1 μg mL^{-1} of MC-LR and 0-30 μg mL^{-1} of the naturally occurring surfactant linear alkylbenzene sulfonate	(Wang et al. 2012)
	Lemna gibba	whole plant	0.016 – 0.911 μg g^{-1} f.w.	Range from exposure to 5-500 μg L^{-1} MC-LR	(Wan et al. 2019)
	Vallisneria natans	seedling	0.053 ± 0.006 μg g^{-1} f.w.	No copper added treatment	(Wang et al. 2017)
	Trapa natans	"meat"	0.001 – 0.007 μg g^{-1} d.w.		(Xiao et al. 2009)
	Vallisneria natans	leaves	0 – 0.35 μg g^{-1} f.w.	Range from treatments of 0.1 – 10,000 μg L^{-1} MC-RR	(Yin et al. 2005)
		root	0.02 – 1.32 μg g^{-1} f.w.		
	Polygonum portoricensis	whole plant	0.58 ± 0.11 μg g^{-1} d.w.		(Romero-Oliva et al. 2014)
	Eichhornia crassipes	whole plant	16.9 ± 2.5 μg g^{-1} d.w.		
	Typha sp.	whole plant	1.6 ± 0.06 μg g^{-1} d.w.		
	Hydrilla verticillata	whole plant	1.4 ± 0.27 μg g^{-1} d.w.		
	Ipomoea aquatica	roots	0.0012 – 0.0021 μg g^{-1} f.w.	Range of values from plants 0.5 – 14.5 meters away from the source water	(Song et al. 2009)
		stem	0.0007 – 0.0014 μg g^{-1} f.w.		
		leaves	0.0007 – 0.0014 μg g^{-1} f.w.		
Epiphyte Concentration	growing on *Elodea candadensis*	Epiphytes	1.16 ± 0.05 μg g^{-1} d.w.	Values extracted from Figure 1 using webplot digitizer	(Mohamed and Al Shehri 2010)
	growing on *Stratiotes aloides*	Epiphytes	3.12 ± 0.4 μg g^{-1} d.w.		
	growing on *Ceratophyllum demersum*	Epiphytes	2.7 ± 0.3 μg g^{-1} d.w.		
	growing on *Myriophyllum verticullatum*	Epiphytes	1.8 ± 0.5 μg g^{-1} d.w.		

Macrophyte Uptake Rate	*Ceratophyllum demersum*	whole plant	3.85 ± 0.29 μg kg^{-1} d.w. d^{-1}	For MC-LR	(Cao et al. 2019)
	Myriophyllum spicatum	whole plant	3.97 ± 0.44 μg kg^{-1} d.w. d^{-1}		
	Vallisneria natans	whole plant	2.88 ± 0.53 μg kg^{-1} d.w. d^{-1}		
	Ceratophyllum demersum	whole plant	1.9 – 331 μg L^{-1} d^{-1}	Range of values for MC-LR only from initial rates at 1 hour into experiment (highest values) to 14 days (lowest values)	(Romero-Oliva et al. 2015)
	Egeria densa	whole plant	2.7 – 544 μg L^{-1} d^{-1}		
	Hydrilla verticillata	whole plant	2.2 – 182.2 μg L^{-1} d^{-1}		
Macrophyte Biotransformation Rate (detoxification)	*Ceratophyllum demersum*	whole plant	1.95 ± 0.06 μg kg^{-1} d^{-1} d.w.	For MC-LR	(Cao et al. 2019)
	Myriophyllum spicatum	whole plant	3.97 ± 0.44 μg kg^{-1} d^{-1} d.w.		
	Vallisneria natans	whole plant	2.16 ± 0.39 μg kg^{-1} d^{-1} d.w.		
	Ceratophyllum demersum	whole plant	3.9 – 672.7 μg L^{-1} d^{-1}	Range of values from initial rates at 1 hour into experiment (highest values) to 14 days (lowest values)	(Romero-Oliva et al. 2015)
	Egeria densa	whole plant	7.1 – 1199 μg L^{-1} d^{-1}		
	Hydrilla verticillata	whole plant	5.4 – 616.5 μg L^{-1} d^{-1}		

Table S6. Microcystin concentrations in aquatic invertebrate tissues.

Pool or Flux	Species	Tissue	Concentration	Citation
Gastropod Tissue Concentration	*Lymnaea stagnalis*	hepatopancreas	80.4 ± 4.9 μg g^{-1} d.w.	(Lance et al. 2006)
	Sinotaia histrica	hepatopancreas	3.2 μg g^{-1} d.w.	(Ozawa et al. 2003)
	Sinotaia histrica	intestine	19.5 μg g^{-1} d.w.	
	Bellamya aeruginosa	hepatopancreas	6.61 μg g^{-1} d.w.	(Zhang et al. 2009)
	Lymnaea stagnalis	whole	0 – 96 μg g^{-1} d.w.	(Kotak et al. 1996)
	Helisoma trivolvis	whole	0 – 11 μg g^{-1} d.w.	
	Physa gyrina	whole	0 – 121 μg g^{-1} d.w.	
	Bellamya aeruginosa	hepatopancreas	2.33 μg g^{-1} d.w.	(Zhang et al. 2007)
		intestine	1.56 μg g^{-1} d.w.	
		gonads	0.38 μg g^{-1} d.w.	
		foot	0.10 μg g^{-1} d.w.	
	Sinotaia histrica	hepatopancreas	1.08 – 8.79 μg g^{-1} d.w.	(Xie et al. 2007)
		intestine	3.74 – 23.2 μg g^{-1} d.w.	
		gonads	0.07 – 22.7 μg g^{-1} d.w.	
		foot	0.04 – 4.45 μg g^{-1} d.w.	
	Physa acuta	unknown	0.06 – 4.15 μg g^{-1} w.w.	(Gérard and Lance 2019)
	Lymnaea stagnalis	unknown	0.002 – 0.008 μg g^{-1} w.w.	(Gérard et al. 2005)
	Assorted species	unknown	0 – 77 μg g^{-1} d.w.	(Zurawell et al. 1999)
	Assorted species	unknown	0 – 4.32 μg g^{-1} d.w.	(Lance et al. 2010)
	Viviparus contectus	whole	0.685 – 1.074 μg g^{-1} d.w.	(Papadimitriou et al. 2012)
	Pleurocera modesta	hepatopancreas	4.29 μg g^{-1} d.w.	(Chen and Xie 2005a)
		gonads	1.17 μg g^{-1} d.w.	
		eggs	0.27 μg g^{-1} d.w.	
		muscle	0.13 μg g^{-1} d.w.	
	Potamopyrgus antipodarum	unknown	0.009 ± 0.005 μg g^{-1} d.w.	(Gérard et al. 2009)
	Planorbis planorbis	unknown	0.006 ± 0.003 μg g^{-1} d.w.	
	Radix auricularia	unknown	0.036 ± 0.012 μg g^{-1} d.w.	

	Radix ovata	unknown	0.008 ± 0.004 μg g^{-1} d.w.	
	Physella acuta	unknown	0.095 ± 0.04 μg g^{-1} d.w.	
	Aplexa hypnorum	unknown	0.006 μg g^{-1} d.w.	
Chironomid Tissue Concentration	*Chironomus sp*.	whole	0.21 – 3.2 μg g^{-1} w.w.	(Toporowska et al. 2014)
	Tanypus chinensis	whole	0 – 12 μg g^{-1} d.w.	(Xue et al. 2016b)
	Chironomus sp.	whole	1.66 – 11.54 μg g^{-1} d.w.	(Chen and Xie 2008)
Decapod Tissue Concentration	*Astacus astacus*	hepatopancreas	0.355 – 0.767 μg g^{-1} d.w.	(Papadimitriou et al. 2012)
		gills	0.405 – 0.701 μg g^{-1} d.w.	
		stomach	0.127 – 0.331 μg g^{-1} d.w.	
		muscle	0.216 – 0.329 μg g^{-1} d.w.	
		brain	0.169 – 0.313 μg g^{-1} d.w.	
		gonads	0.114 – 0.302 μg g^{-1} d.w.	
	White shrimp	hepatopancreas	55 μg g^{-1}	(Zimba et al. 2006)
		muscle	<0.1 μg g^{-1}	
	Freshwater shrimp	unknown	55 μg g^{-1}	(Galanti et al. 2013)
	Atyaephyra desmaresti	whole	0.75 – 2.25 μg g^{-1} d.w.	(Papadimitriou et al. 2012)
	Macrobrachium nipponesis	hepatopancreas	0 – 24 μg g^{-1} d.w.	(Zhang et al. 2009)
	Macrobrachium nipponesis	hepatopancreas	0.53 μg g^{-1} d.w.	(Chen and Xie 2005a)
		gonads	0.48 μg g^{-1} d.w.	
		eggs	2.34 μg g^{-1} d.w.	
		muscle	0.04 μg g^{-1} d.w.	
Bivalve Tissue Concentration	*Coricula fluminea*	hepatopancreas	0 – 5.18 μg g^{-1} d.w.	(Chen and Xie 2008)
		intestine	0 – 1.16 μg g^{-1} d.w.	
		muscle	0 – 0.18 μg g^{-1} d.w.	
		whole body	0 – 0.53 μg g^{-1} d.w.	
	Arconaia lanceolata	hepatopancreas	18.01 μg g^{-1} d.w.	
	Anodonata woodiana	hepatopancreas	1.54 μg g^{-1} d.w.	(Chen and Xie 2005b)
	Cristaria plicata	hepatopancreas	5.79 μg g^{-1} d.w.	(Chen and Xie 2007)
		whole body	10.74 μg g^{-1} d.w.	
	Hyriopsis cumingii	hepatopancreas	3.42 μg g^{-1} d.w.	

		whole body	6.17 µg g^{-1} d.w.	
	Lamprotula leai	hepatopancreas	4.25 µg g^{-1} d.w.	
		whole body	8.71 µg g^{-1} d.w.	
	Sphaerium corneum	whole body	0.003 ± 0.002 µg g^{-1} w.w.	(Gérard et al. 2009)
	Pisidum sp.	whole body	0.013 ± 0.006 µg g^{-1} w.w.	
	Unio douglasiae	muscle	11.2 – 70.1 µg g^{-1} d.w.	(Kim et al. 2017)
		gland	0.17 – 0.87 µg g^{-1} d.w.	
	Sinanodonata woodiana	muscle	0.083 – 0.767 µg g^{-1} d.w.	
		gland	0.006 – 0.031 µg g^{-1} d.w.	
	Sinanodonata arcaformis	muscle	0.006 – 0.022 µg g^{-1} d.w.	
		gland	0.061 – 0.655 µg g^{-1} d.w.	
	Dreissenia polymorpha	unknown	11 µg g^{-1} d.w.	(Pires et al. 2004)
	Anodonata grandis simpsoniana	unknown	0.024 – 0.527 µg g^{-1} d.w.	(Prepas et al. 1997)
	Anodonta cygnea	hepatopancreas	0.885 – 1.347 µg g^{-1} d.w.	(Papadimitriou et al. 2012)
		stomach	0.383 – 1.189 µg g^{-1} d.w.	
		mantle	0.034 – 1.151 µg g^{-1} d.w.	
		foot	0.799 – 1.172 µg g^{-1} d.w.	
	Unio douglasiae	hepatopancreas	130 – 250 µg g^{-1} d.w.	(Yokoyama and Park 2003)
	Anodonata woodiana	whole body	12.6 µg g^{-1} d.w.	(Yokoyama and Park 2002)
	Cristaria plicata	hepatopancreas	297 µg g^{-1} d.w.	
	Unio douglasiae	hepatopancreas	420 µg g^{-1} d.w.	
Oligochaete Tissue Concentration	*Limnodrilus hoffineisteri*	whole	0.3 – 11.99 µg g^{-1} d.w.	(Xue et al. 2016a)
	Limnodrilus hoffineisteri	whole	0.23 µg g^{-1} d.w.	(Chen and Xie 2008)
Zooplankton Tissue Concentration	Zooplankton	whole	80 – 152 µg g^{-1} d.w.	(Papadimitriou et al. 2012)
	Zooplankton	whole	0 – 67 µg g^{-1} d.w.	(Kotak et al. 1996)
	Daphnia pulicaria	whole	74 - 1099 µg g^{-1} d.w.	(Oberhaus et al. 2007)
	Daphnia similis	whole	184 µg g^{-1} d.w.	(Ferrão-Filho et al. 2014)
	Daphnia laevis	whole	1260 µg g^{-1} d.w.	
	Moina micrura	whole	1170 µg g^{-1} d.w.	
	Cyclops vicinus	whole	0.05 – 3.21 µg individual	(Mohamed et al. 2018)

Table S7. Microcystin concentration in vertebrate tissues (aquatic and terrestrial).

Pool or Flux	Species	Tissue	Concentration	Notes	Citation
Fish Tissue Concentrations	Wild caught freshwater fish, multiple species (ranges from meta-analysis of concentrations)	muscle	0 – 3.27 μg g^{-1} d.w	n = 1,035 data points	(Flores et al. 2018)
		liver	0 – 375.3 μg g^{-1} d.w	n = 554 data points	
		hepatopancreas	0.34 – 1.62 μg g^{-1} d.w	n = 15 data points	
		intestine	0 – 7.44 μg g^{-1} d.w	n = 77 data points	
		gill	0 – 0.13 μg g^{-1} d.w	n = 13 data points	
		kidney	0 – 14.14 μg g^{-1} d.w	n = 93 data points	
		brain	0 – 2.07 μg g^{-1} d.w	n = 42 data points	
		blood	0.62 – 46.98 μg g^{-1} d.w	n = 9 data points	
		gut	0.001 – 2.67 μg g^{-1} d.w	n = 31 data points	
		spleen	0 – 2.06 μg g^{-1} d.w	n = 16 data points	
		gallbladder	0 – 0.23 μg g^{-1} d.w	n = 16 data points	
		whole	0.003 – 0.69 μg g^{-1} d.w	n = 25 data points	
		viscera	0.02 – 8.86 μg g^{-1} d.w	n = 8 data points	
		belly flap	0.02 – 0.98 μg g^{-1} d.w	n = 29 data points	
		heart	0 – 0.09 μg g^{-1} d.w	n = 16 data points	
Amphibian Tissue Concentrations	*Rana epirotica*	liver	0.209 – 0.581 μg g^{-1} d.w.		(Papadimitriou et al. 2012)
		pancreas	0.142 – 0.554 μg g^{-1} d.w.		
		intestine	0.103 – 0.321 μg g^{-1} d.w.		
		skin	0.081 – 0.419 μg g^{-1} d.w.		
		muscle	0.088 – 0.326 μg g^{-1} d.w.		
		gonads	0.069 – 0.165 μg g^{-1} d.w.		
Reptile Tissue Concentrations	*Crocodylus niloticus*	eggs	0 – 0.002 μg g^{-1} d.w.		(Singo et al. 2017)
	Mauremys leprosa	viscera	90.25 μg g^{-1} d.w.	Lemieux oxidation-GC/MS method	(Nasri et al. 2008)
		liver	1192.8 μg g^{-1} d.w.		
		muscle	10.13 μg g^{-1} d.w.		
	Emys orbicularis	viscera	37.2 μg g^{-1} d.w.		
		liver	23.8 μg g^{-1} d.w.		
		muscle	9.4 μg g^{-1} d.w.		
	Pelodiscus sinensis	liver	0.021 μg g^{-1} d.w.		(Chen et al. 2009)

		intestine	0.020 µg g^{-1} d.w.	
		gonad	0.002 µg g^{-1} d.w.	
		muscle	0.006 µg g^{-1} d.w.	
		other organs	0.033 µg g^{-1} d.w.	
Bird Tissue Concentrations	*Anas platyrhynchos*	liver	0.030 µg g^{-1} d.w.	
		intestine	0.051 µg g^{-1} d.w.	
		gonad	0.009 µg g^{-1} d.w.	
		muscle	0.016 µg g^{-1} d.w.	
		other organs	0.062 µg g^{-1} d.w.	
	Nycticorax nyctincorax	liver	0.018 µg g^{-1} d.w.	
		intestine	0.082 µg g^{-1} d.w.	
		gonad	0.010 µg g^{-1} d.w.	
		muscle	0.003 µg g^{-1} d.w.	
		other organs	0.064 µg g^{-1} d.w.	
	Phoeniconaias minor	liver	18.27 ± 16.9 µg g^{-1} w.w.	(Nonga et al. 2011)
	Anas platyrhynchos	liver	0.172 – 0.272 µg g^{-1} w.w.	(Foss et al. 2018)
	Coturnix japonica	liver	0.037 – 0.061 µg g^{-1} w.w.	(Pikula et al. 2010)
Mammal Tissue Concentration	*Canus lupus familiaris*	liver	>1 µg g^{-1} d.w.	(van der Merwe et al. 2012)

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