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Occurrence and Mass Flows of Organic Micropollutants in the Onondaga Lake – Three Rivers System

Shiru Wang
Syracuse University

Abstract

Organic micropollutants (OMPs) are synthetic and naturally occurring organic compounds that may pose long-term ecotoxicological risks to the aquatic life occur at low levels. This work seeks to characterize the spatiotemporal occurrence and mass flows of OMPs in the Onondaga Lake-Three Rivers system in central New York. In collaboration with the Upstate Freshwater Institute, multiple batches of water samples were collected from the lake-river system between June and October 2017 and analyzed for OMPs using a suspect screening workflow developed on liquid chromatography-high resolution mass spectrometry. To date, a total of 52, 31, and 37 OMPs were identified and quantified in Onondaga Lake, its four major tributaries, and the Three Rivers, respectively. Lamotrigine, estradiol, benzotriazole, methyl benzotriazole, sucralose, and atrazine were measured in every sample, suggesting their ubiquitous presence in the lake-river system. Over the study period, the horizontal concentration profiles of OMPs in Onondaga Lake showed relatively consistent patterns, but the vertical distribution of OMPs in the lake was influenced by thermal stratification and wastewater discharge from a regional WWTP serving the Syracuse metropolitan area. Specifically, OMPs derived from point source wastewater discharge exhibited peak concentrations in the thermocline in July 2017, but such phenomenon disappeared in October 2017, likely due to changes in lake stratification. OMPs were generally detected at lower levels in the lake tributaries and the Three Rivers, suggesting diffuse inputs from agricultural activities or irregular wastewater discharge. Further calculations of the OMP mass flow revealed that the WWTP might account for up to 67-86% of the OMP mass flow entering the lake, which is in line with its high percentage of wastewater inflow. Onondaga Lake itself contributed 12-24% of the OMP mass flow entering the Three Rivers, confirming its role as a regionally important source of OMPs.

Occurrence and Mass Flows of Organic Micropollutants in the Onondaga Lake – Three Rivers System

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Shiru Wang

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Chapter 1: Introduction

1.1 Occurrence and Fate of Organic Micropollutants

Organic micropollutants (OMPs) comprise a wide array of synthetic (i.e., man-made) and naturally occurring organic chemicals that are detected with increasing frequency at low concentrations in the aquatic environment and are thought to have the potential to cause adverse effects on ecosystem functioning.[1] OMPs can be broadly categorized into anthropogenic organic compounds (e.g., human-use pharmaceuticals, personal care products, veterinary drugs) and biogenic toxins (e.g., algal toxins produced by harmful algal blooms) that have not yet been regulated for environmental impacts, as shown in Table 1. In the U.S., monitoring of OMPs in the aquatic environment does not routinely occur, and regulatory efforts to prevent OMPs from entering the environment remain rather limited. Thus, managing the ever-growing amount and variety of OMPs has become a key challenge for regulators and scientists. Recognizing the need for additional data for risk assessment, the U.S. Geological Survey (USGS) and the U.S. Environmental Protection Agency (USEPA) have initiated a series of large-scale monitoring campaigns targeting a broad suite of OMPs in surface and groundwaters across the U.S. During 1999 and 2000, a nationwide reconnaissance led by the USGS first reported the presence of 95 pharmaceuticals, hormones, and other OMPs in 80% of the 139 streams surveyed across 30 states, providing one of the earliest evidence for surface water contamination by OMPs in North America.[2] Since then, significant efforts have been made to characterize the occurrence, fate, transport, and ecotoxicological effects of OMPs.[3–12] During 2012 and 2014, the USGS and USEPA launched a follow-up nationwide study to investigate the prevalence of 719 OMPs in 38 U.S. streams and reported that 406 of the targeted OMPs were detected at least once, with eight

pesticides and two pharmaceuticals being the 10 most-frequently detected OMPs across all sites.[13] In New York State, OMPs have been detected in the public water supplies, recreational waters, and other environmental compartments. For instance, previous studies have measured a variety of OMPs in the Hudson River Estuary Cantwell,[14,15] the Croton Reservoir system,[16] the Lake Champlain basin,[12] and Long Island.[17,18] However, a systems approach is still needed to inform future research on the occurrence and effects of OMPs and to address challenges associated with the risk-driving substances.

Table 1. Major categories and examples of OMPs reported in the literature

Category	**Examples**
Human-use pharmaceuticals	Prescription and over-the-counter drugs, Drugs of abuse
Personal care products	UV filters, Antimicrobial agents, Plasticizers
Household chemicals	Surfactants, Flame retardants
Food additives	Artificial sweeteners, Stimulants
Agricultural pesticides	Herbicides, Insecticides, Fungicides
Veterinary drugs	Hormonal growth promoters, Antiparasitic agents
Industrial chemicals	Per- and polyfluoroalkyl substances, Corrosion inhibitors
Algal toxins	Microcystins, Anatoxins, Cylindrospermopsins

With the aging population in the developed countries and ongoing increases in the living standard in developing regions, the global production and consumption of pharmaceuticals has continued to increase over the past century and is projected to increase substantially in coming decades.[19,20] More than 3000 pharmaceuticals are currently approved for prescription in the U.S., while hundreds of others are approved for over-the-counter use or used in related formulations.[21] Pharmaceutically active ingredients contained in human-use pharmaceuticals and veterinary drugs have been identified as a major group of OMPs occurring in the aquatic environment.[22,23] Since the late 1990s, numerous studies have reported the widespread occurrence of

pharmaceuticals at ng/L to µg/L levels in surface and groundwaters, particularly those receiving urban wastewater inputs.[24] Over 630 pharmaceuticals and their transformation products have been identified in environmental water samples across 71 countries on all continents except Antarctica.[24] Sixteen pharmaceuticals, including 5 antibiotics, 5 analgesics, 4 estrogens, and 2 other therapeutic drugs, were found in the surface waters and groundwater across all regions, with some of the highest concentrations at mg/L levels downstream of pharmaceutical manufacturing facilities.[24] A nationwide study led by the USEPA examined 182 sampling sites representing ~30,000 km of fifth order and higher urban streams and reported the occurrence of 37 antibiotics, diuretics, antihypertensives, anticonvulsants, and antidepressants with the maximum concentration reaching up to 620 ng/L.[25] Simultaneously, another nationwide reconnaissance led by the USGS investigated 35 human-use pharmaceuticals and veterinary drugs at 47 groundwater sites across 18 states and highlighted antibiotics as the most frequently detected group of compounds.[26] Recently, a joint study conducted by the USEPA and USGS revealed the presence of 118 pharmaceuticals in wastewater-impacted source waters serving 25 drinking water treatment plants across the U.S.[27] Similar to the findings from these national surveys, recent studies in New York State have measured pharmaceuticals in source waters. For example, a study conducted by the New York State Department of Health found low ng/L levels of antibiotics, antihypertensives, and analgesics in Skaneateles Lake, the major source of drinking water for ~200,000 residents in and around the City of Syracuse.[28] Another recent study conducted by the USGS New York Water Science Center detected several pharmaceuticals in the shallow groundwater downgradient of septic systems on Long Island.[29]

With the rapid agricultural expansion and intensification, the global production and application of pesticides have increased drastically between the 1950s and 2000s[30], which has

posed significant threats to the ecological integrity of aquatic and terrestrial ecosystems (e.g., decreasing regional aquatic biodiversity).[31,32] More than 900 pesticides have been registered for use in the U.S. since 1967, and approximately 1 billion pounds of pesticides are consumed annually to control weeds, insects, fungi, and other pests.[33] Active pesticide ingredients, such as formulated herbicides, insecticides, and fungicides, are applied extensively over large areas in agriculture and urban settings, thereby representing another major group of OMPs commonly found in the aquatic environment. The USGS National Water-Quality Assessment (NAWQA) Program has conducted a decadal assessment of the occurrence of pesticides in streams and shallow groundwater during 1992 and 2011. Pesticides and their transformation products were detected >90% of the time of the year in streams that have watersheds dominated by agricultural, urban, and mixed land use, with 11 herbicides, 4 insecticides, and 1 fungicide being the most frequently detected compounds.[34] Notably, the concentrations of seven pesticides (i.e., metolachlor, atrazine, diazinon, malathion, chlorpyrifos, carbaryl, and fipronil) in streams frequently exceeded water-quality benchmarks for aquatic life or fish-eating wildlife, despite the variability of seasonal patterns and multiyear trends over the 20-year period.[34] Pesticides were less commonly detected in groundwater, but still occurred in >50% of the sampled shallow groundwater wells in agricultural and urban areas, with triazines and chloroacetanilides being the most frequently detected.[33]

Besides pharmaceuticals and pesticides, many other synthetic and naturally-occurring compounds constitute the majority of OMPs due to their potential for causing adverse ecotoxicological effects and the increasing number of studies that report their occurrence in the environment. For example, personal care products, such as soaps, skin care products, toothpaste, and sunscreens, are normally used in larger quantities than recommended and enter the aquatic

environment unaltered through normal human usage.[35–37] Chemical additives used in the personal care products, such as disinfectants, fragrances, preservatives, and UV filters, are among the most commonly detected OMPs in surface waters worldwide and often occur at higher concentrations than pharmaceuticals. The nationwide reconnaissance led by the USGS detected 7 plasticizers, 1 disinfectant, 1 fragrance, and 5 detergent metabolites in 139 streams across 30 states and reported that triclosan (an antimicrobial agent) was one of the most frequently detected OMPs with concentrations as high as 2.3 μg/L.[38] A subsequent study further identified the co-occurrence of triclocarban, another antimicrobial agent, with triclosan in six urban streams in the Greater Baltimore region with a detection frequency above 60%.[39]

Given the widespread occurrence of OMPs in the aquatic environment, it is necessary to characterize their sources and transport pathways to inform monitoring efforts and management strategies.[40] Wastewater and terrestrial runoff (e.g., agricultural and urban runoff) are important sources of OMPs. In urban areas, OMPs most likely originate from municipal wastewater effluents discharged by wastewater treatment plants (WWTPs), combined sewer overflows, industrial wastewater effluents, or stormwater runoff.[41,42] Among these, wastewater effluents normally serve as the most significant source of OMPs because many OMPs are poorly removed by treatment processes used in WWTPs.[40] Furthermore, OMPs may enter shallow groundwater via leaking sewer networks.[6] Thus, wastewater-derived OMPs, such as human-use pharmaceuticals, personal care products, and household chemicals, often have high detection frequencies and concentrations in the urban water cycle. In agricultural areas, OMPs typically originate from runoff (e.g., during preferential flow events) generated by agriculture-related activities, such as pest management, concentrated animal feeding operations, and the application

of manure and biosolids. OMPs may also leach to shallow groundwater once released into the soil.

OMPs can undergo abiotic (i.e., not involving metabolically-active organisms) and/or biotic (i.e., mediated by microorganisms or plants) transformations upon release into the environment, although many OMPs are considered persistent or "pseudo-persistent" because either they degrade very slowly in the environment or their constant use leads to continuous release into the environment at rates exceeding their degradation rates.[20] Common transformation processes in natural systems include hydrolysis, reduction-oxidation (redox) reactions, direct and indirect photolysis, and biotransformation. What transformation processes a given OMP undergoes is governed by its structural characteristics (e.g., reactive sites susceptible to certain reactions) and the prevailing environmental conditions it is exposed to as a result of its partitioning behavior.[3] For instance, photolysis is typically restricted to compartments exposed to sunlight (e.g., the photic zone of lakes or streams). Redox reactions in soils, sediments, or aquifers are often driven by the availability of oxygen. While most transformation processes generate benign transformation products (TPs), past research has highlighted cases where TPs can occur at higher concentrations than their parent compounds[43] or even retain equal or create greater bioactivity[44]. One classical example is the photochemical condensation of triclosan (an antimicrobial agent) and its chlorinated derivatives, which generates dioxin-like products that accumulate in the sedimentary environment.[45] Another prominent example is the photohydration of the metabolites of trenbolone (a high-value steroidal growth promoter), which yields products that not only retain bioactivity but also undergo further dehydration to regenerate the parent steroid in the dark.[46]

In parallel to the natural aquatic systems, many studies have also demonstrated the formation of TPs during drinking water and advanced wastewater treatment processes.[3] Oxidative treatment processes, such as ozonation, chlorination, and UV/hydrogen peroxide-based advanced oxidation, are known to form a variety of unknown TPs.[3,22,47] For example, chlorination, the most widely used disinfection method in the U.S., promotes the formation of a wide array of halogenated disinfection byproducts (e.g., trihalomethanes, haloacetic acids, haloacetonitriles, haloacetamides, haloacetaldehydes, and halonitromethanes) that exhibit cytotoxicity and/or genotoxicity.[3,22] Ozonation, which is gaining popularity in Europe for post-treatment of municipal wastewater, promotes the formation of bromate, which is considered to be a probable human carcinogen [48]. Collectively, existing literature has shown that the co-existence of TPs with parent compounds is clearly an important consideration for a more complete environmental risk assessment of OMPs.

1.2 Potential Ecotoxicological Risks of OMPs

Exposure to OMPs has been linked to some undesirable ecological effects such as endocrine disruption and induction of antibiotic resistance. Endocrine disruption interferes with the proper functioning of an organism's endocrine system that is responsible for regulating hormones.[49–51] Some OMPs are potent endocrine disruptors that pose effects such as behavioral changes, reproductive disruption[52–54], and even population crashes[55] of aquatic organisms. For instance, a study conducted in eight rivers in U.K. first documented that exposure to the ambient level of estrogenic chemicals caused the adverse reproductive health effects in a cyprinid fish.[52] The Fisheries and Oceans Canada further demonstrated that the addition of ng/L levels of ethinylestradiol significantly decreased the reproductive success and sustainability of fish populations in an experimental lake.[55] Antibiotic resistance is the ability of bacteria to survive

exposure to antibiotics and continue to multiply, potentially causing more harm and spreading to humans or other organisms. Previous studies have established that longer-term exposure to ecologically relevant concentrations of antibiotics could lead to increased antibiotic resistance in microbial populations.[56,57] For example, a recent study showed that exposure to 4 antibiotics induced the biofilm functioning resistance in several urban streams in Baltimore, MD.[57] Despite their low concentrations, the ecotoxicological relevance of OMPs cannot be overlooked. However, quantifying the environmental effects of OMPs, especially in realistic mixture scenarios, remains challenging because of the limited availability of biochemical data to infer the impacts of specific OMPs in complex mixtures.

1.3 Analytical Techniques

Given the widespread occurrence and potential ecotoxicological effects of OMPs, a number of novel screening and prioritization methods have been developed in recent years to study the occurrence and fate of OMPs in the aquatic environment.[5,58–61] With its high resolution power and mass accuracy, high resolution mass spectrometry (e.g., time-of-flight or Orbitrap) coupled to liquid chromatography with electrospray ionization (hereafter referred to as "LC-HRMS") has proven to be a superior analytical platform for screening and quantification of OMPs at environmentally relevant concentrations in complex matrices.[62] Typically, LC-HRMS analysis acquires full scan mass spectral data plus tandem mass fragmentation information that aids in structural elucidation. Target screening, suspect screening, and non-target screening based on LC-HRMS (Figure 1) are the three strategies commonly used to identify and quantify OMPs in various environmental samples.[63]

Target screening has been the gold standard for quantitative OMP monitoring and is routinely implemented for large-scale occurrence studies.[64] This approach pre-selects a limited number of OMPs based on expert knowledge and analytical feasibility and relies on authentic reference standards to generate compound-specific information such as retention times and tandem mass fragmentation patterns for confirmation and quantification of OMPs.[65] Purchasing all the reference standards without knowledge about OMPs potentially present in the system of interest is economically inefficient, and may underestimate the extent of contamination and associated risks.[63,66,67] Furthermore, many reference standards are currently not available for emerging substances, in particular, transformation products. Existing target screening methods also need to be constantly re-evaluated as additional reference standards are purchased to accommodate new research objectives or the changing environment,[63] Despite these drawbacks, target screening remains a powerful approach for comprehensive screening of OMPs in the environment, especially when multiple methods are used in combination.[13]

Non-target screening has recently emerged as an important tool for identifying all detectable OMPs in samples without any *a priori* information.[63,65,66] This approach provides a more holistic picture of OMPs with less bias caused by pre-selection of known substances. Many studies employing non-target screening have aimed at identifying unknown or unexpected OMPs for treatment process assessments and pollutant prioritization. Typically, hundreds to thousands of mass spectral features can be identified in a single sample, making manual data processing no longer an efficient option. Instead, semi-automated processing strategies are needed to reduce the complexity of compound identification, while minimizing false positive and false negative findings. To date, the identification of unknown OMPs remains a difficult and time-consuming task with no guarantee of success. Starting with peak picking, exact mass matching, and isotope

pattern scoring, a list of candidate structures can be retrieved via online compound databases for any given unknown feature.[68,69] Compound databases either contain structures and properties of millions of synthetic or natural chemicals (e.g., PubChem and ChemSpider) or searchable tandem mass spectra of organic compounds (e.g., METLIN, MassBank, and mzCloud). Recent studies have combined the use of these compound databases with computational tools such as *in silico* fragmentation and/or retention time prediction to achieve tentative identification of unknown OMPs without reference standards. However, rigorous and systematic prioritization strategies are still critical when it comes to selecting the most relevant candidate structures in samples for unknown identification because many features must be evaluated irrespective of the research objective.[66,70–72] Furthermore, authentic reference standards or orthogonal techniques (e.g., nuclear magnetic resonance spectroscopy) are required for unequivocal confirmation of unknown OMPs.[62] Ultimately, previously-unknown OMPs discovered through non-target screening efforts can be included for target screening in future investigations.

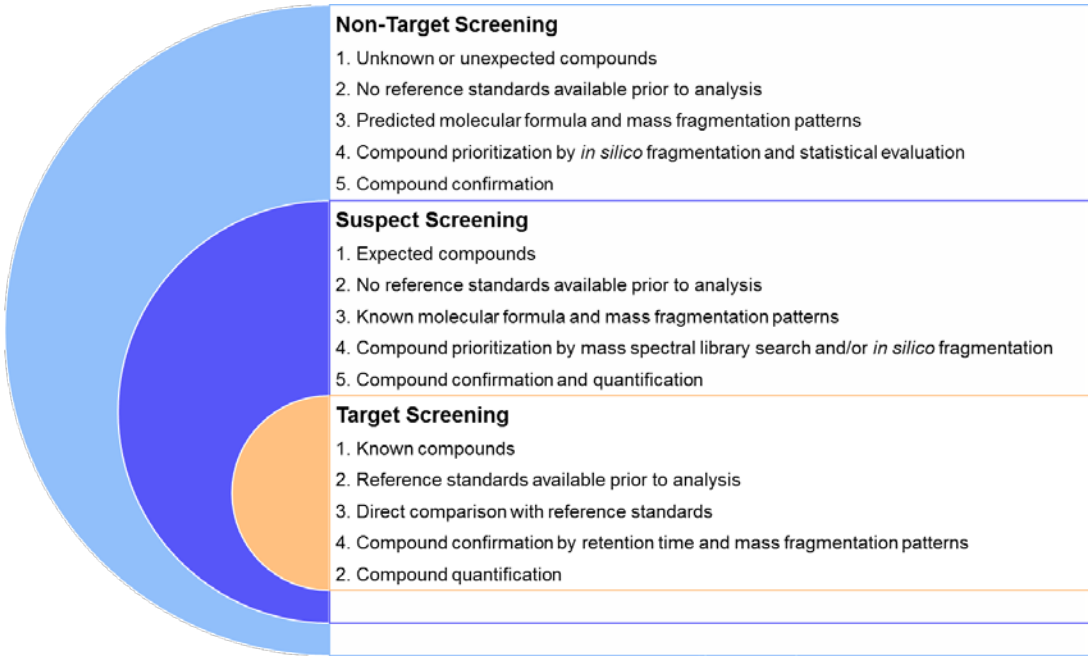

Figure 1. Three LC-HRMS screening strategies used for analysis of OMPs in environmental samples.

Suspect screening without authentic reference standards is an efficient screening approach that links the mass spectral features to an extensive list of expected OMPs with compound-specific information such as exact masses and molecular structures.[63,64,67,73] One key advantage of suspect screening as compared to target or non-target screening is utilizing suspect compound databases to help focus screening efforts on OMPs that have high possibility to occur in samples while achieving a reasonably comprehensive coverage. Expert knowledge (e.g., previous monitoring data, production volume, environmental fate properties) regarding OMPs likely to occur in the system of interest is essential for compiling suspect databases and ultimately the effectiveness of the suspect screening workflow.[62,65] Similar to non-target screening, prioritization strategies need to be systematically optimized with known OMPs to achieve a rapid and comprehensive characterization of OMPs for further confirmation.

1.4 Onondaga Lake - Three Rivers System

Onondaga Lake is located in central New York immediately northwest of the City of Syracuse (latitude 43°06’54”, longitude 76°14’34”). The lake has a longitudinal axis measuring ~7.6 km, a surface width ranging between 1-2 km, and a surface area of 11.7 km^2. The mean depth of the lake is 10.9 m, with a maximum of 19.5 m. The bathymetry of the lake is characterized by two minor depressions, referred to as the northern and southern basins, separated by a shallower region near the center of its longitudinal axis. Onondaga Lake drains a highly urbanized watershed covering approximately 725 km^2.[74–76] The major hydrologic inputs to Onondaga Lake are four tributaries (i.e., Ninemile Creek, Onondaga Creek, Ley Creek, and Harbor Brook) and a regional wastewater treatment plant (WWTP) that serves the Syracuse metropolitan area. Onondaga Lake discharges through a single outlet at its northern end to the Seneca River, which flows northerly and joins the Oneida River to form the Oswego River that

ultimately enters Lake Ontario at the City of Oswego.[77] The Three Rivers (i.e., Seneca-Oneida-Oswego) system is the largest river network in central New York, with the Oswego River being the second largest tributary to Lake Ontario (after the Niagara River).[74] The Three Rivers is an integral part of the New York State Barge Canal System and provides services including recreation, navigation, power generation, and waste discharge.[77]

Onondaga Lake was historically the most polluted lake in the U.S. and has received both treated and untreated industrial (e.g., soda ash, heavy metals, PCBs, PAHs) and domestic waste for over a century.[78] Notably, more than 75 metric tons of Hg associated with chlor-alkali production was discharged into the lake before 1970, leading to chronic contamination of its water column, sediments, and biota. Because of the extensive Hg pollution, Onondaga Lake and related upland sites were added to the EPA Superfund National Priority List in 1994. Since then, Superfund remediation of Hg has dramatically improved the lake's water quality.[74,78,79] While the remediation of Onondaga Lake has achieved great success, the public remains concerned about the lake water quality. Today, Onondaga Lake is still stressed by pollution from point sources such as wastewater discharge and diffuse inputs from urban runoff. Particularly, wastewater effluent discharged from the regional WWTP accounts for 20-30% of the annual hydrologic budget for the lake, representing the most significant source of wastewater in the Three Rivers system. This contribution of wastewater effluent to total inflow for Onondaga Lake is among the highest for a lake in the U.S. Under wet weather conditions, combined sewer overflows represent another potential contributor of raw wastewater into Onondaga Lake. Given the known wastewater input, a broad suite of OMPs likely enter Onondaga Lake and the Three Rivers. To date, no data exist with respect to the spatiotemporal occurrence and mass flows of OMPs in this lake-river system. Without this knowledge, assessing the potential environmental

effects of OMPs or developing future monitoring programs and pollution mitigation strategies will be hindered.

1.5 Objective and Hypotheses

The primary objective of this thesis is to characterize the spatiotemporal occurrence and mass flows of OMPs in the Onondaga Lake-Three Rivers system using a suspect screening method developed on liquid chromatography-high resolution mass spectrometry. The hypotheses are (1) wastewater effluent represents a major source of OMPs in Onondaga Lake; (2) the occurrence patterns of OMPs differ depending on their sources; and (3) Onondaga Lake plays an important role in contributing OMPs to the Three Rivers System. To test these hypotheses, we (1) collected grab water samples from Onondaga Lake, its tributaries, and Three Rivers from June to October 2017 in collaboration with the Upstate Freshwater Institute (UFI); (2) developed and optimized a suspect screening workflow for OMP analysis in the lake and river water samples; (3) applied suspect screening to identify and quantify OMPs present in the lake-river system; and (4) estimated the mass flows of OMPs in the lake-river system.

Chapter 2: Materials and Methods

2.1 Field Sampling

A total of 139 water samples and corresponding field blanks were collected by the Upstate Freshwater Institute (UFI) from the Onondaga Lake-Three Rivers system between June and October 2017 under dry weather conditions. The UFI is a not-for-profit 501(C)(3) research corporation that conducts long-term water quality research in Onondaga Lake and other freshwater systems in New York State. Grab samples were collected using aged fluorinated high-

density polyethylene bottles and transported on ice to Syracuse University as soon as practically possible. While grab samples may not be able to reflect the time-integrated dynamics of OMP occurrence, repeated grab sampling has been shown to provide robust estimates of mean OMP concentrations at a given site.[15] Eight batches of samples were collected biweekly from four sites (i.e., L1 (South End), L2 (South Deep), L3 (North Deep), and L4 (Outlet)) along the longitudinal axis of Onondaga Lake and from the mouths of its four major tributaries (i.e., T1 (Ninemile Creek), T2 (Onondaga Creek), T3 (Harbor Brook), and T4 (Ley Creek)), as illustrated in Figure 2. Because Onondaga Lake is thermally stratified between late May and late October,[74] paired samples were collected from two different depths (i.e., 1-m below the surface and 2-m above the bottom) at sites L2 and L3. Two batches of depth profile samples were also collected with 1-m depth intervals at site L2 in July and October 2017, respectively. Site L2 is the long-term sampling site for the lake and is generally representative of lakewide conditions.[80] Water quality parameters, such as temperature, specific conductance, pH, and dissolved oxygen (DO), were monitored in real time by a robotic monitoring buoy located at site L2. Two batches of samples were collected from the Three Rivers system in July and October 2017. Three sites were sampled on the Seneca River, with one (site R1) located upstream of Onondaga Lake outlet and two others (sites R2 and R3) located downstream of Onondaga Lake outlet but upstream of the Seneca-Oneida confluence. One site (site R4) was sampled at the mouth of the Oneida River. Eight additional sites (sites R5 to R12) were sampled along the Oswego River downstream of the Seneca-Oneida confluence prior to its entry into Lake Ontario. Key ancillary water quality parameters (e.g., temperature, specific conductance, pH, dissolved oxygen, and turbidity) were measured by the UFI scientists with rapid profiling instrumentation.

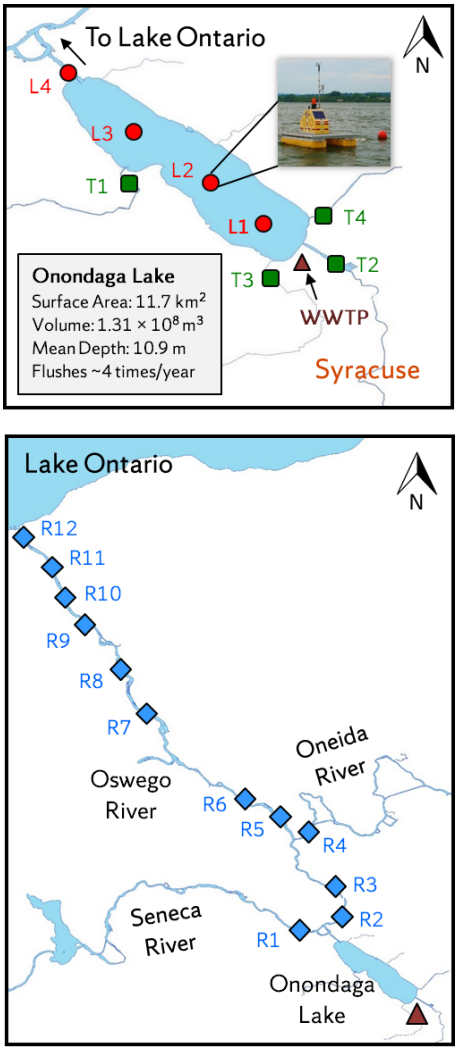

Figure 2. Map of the sampling sites in the Onondaga Lake, its tributaries, and the Seneca-Oneida-Oswego Rivers. The insect map is the map of the sampling sites in the Onondaga Lake and tributaries. The red dots represent the sampling locations in Onondaga Lake. The green squares represent the sampling locations on the lake tributaries. The blue rhombus represent the sampling locations on the Three Rivers. The brown triangle represents the WWTP serving the Syracuse metropolitan area. The inset photo in the upper panel shows the monitoring buoy at site L2 and is courtesy of the Upstate Freshwater Institute.

2.2 Laboratory Analysis

Reference standards of OMPs (purity >98%) were purchased from Sigma-Aldrich (St. Louis, MO), Toronto Research Chemicals (North York, ON, Canada), and AccuStandard (New Haven, CT), and stored under recommended conditions until use. Twenty-three isotope-labeled internal standards were purchased from CDN Isotopes (Pointe-Claire, QC, Canada). Stock

solutions of reference standards were prepared in LC-MS grade water, methanol, or acetonitrile, and stored in the dark under -20 °C until use. LC-MS grade water, methanol, ethyl acetate, formic acid, and ammonium hydroxide were purchased from Fisher Scientific (Waltham, MA).

2.2.1 Solid-Phase Extraction

Upon return to the laboratory, water samples were vacuum filtered through 0.7-µm glass fiber filters to remove suspended particulate matter. Filtered water samples were buffered at pH 6.8 with formic acid, spiked with a mixture of isotope-labeled internal standards (100 ng per 500 mL sample), and passed through dual solid-phase extraction (SPE) cartridges to enrich a broad range of neutral, cationic, and anionic OMPs, as shown in Figure 3. Two different sets of 15-mL SPE cartridges were manually packed in-house according to Schollée et al. 2015 with modifications.[58] The mixed-mode SPE cartridges contained four sorbents, including 200 mg of Phenomenex Sepra ZT, 100 mg of Phenomenex Sepra ZT-SAX, 100 mg of Phenomenex Sepra ZT-SCX, and 150 mg of Biotage ISOLUTE ENV+. The single-mode SPE cartridges contained 200 mg of Enviro-Clean graphitized nonporous carbon. Prior to extraction, the mixed-mode and single-mode cartridges were connected (with the mixed-mode on top) and conditioned with 15 mL of methanol followed by 30 mL of deionized water. Water samples were transferred by large volume samplers from volumetric flasks and passed through the dual cartridges at a flow rate of ~5 mL/min. Following extraction, the cartridges were dried for 15 min under vacuum, reconnected (with the single-mode on top), and eluted sequentially with 6 mL of methanol/ethyl acetate (50:50 v/v) amended with 2% ammonia, 3 mL of methanol/ethyl acetate (50:50 v/v) amended with 1.7% formic acid, and 2 mL of methanol. The combined solvent extracts were concentrated to 2-3 mL using a BUCHI R-100 rotary evaporator, further evaporated to 100 µL under high-purity N_2, and reconstituted with methanol:water (10:90 v/v) to a final volume of 1

mL.[81] All final sample extracts were stored in the dark under -20 °C until analysis. Field blanks and calibration standards were extracted following the same protocol as described above.

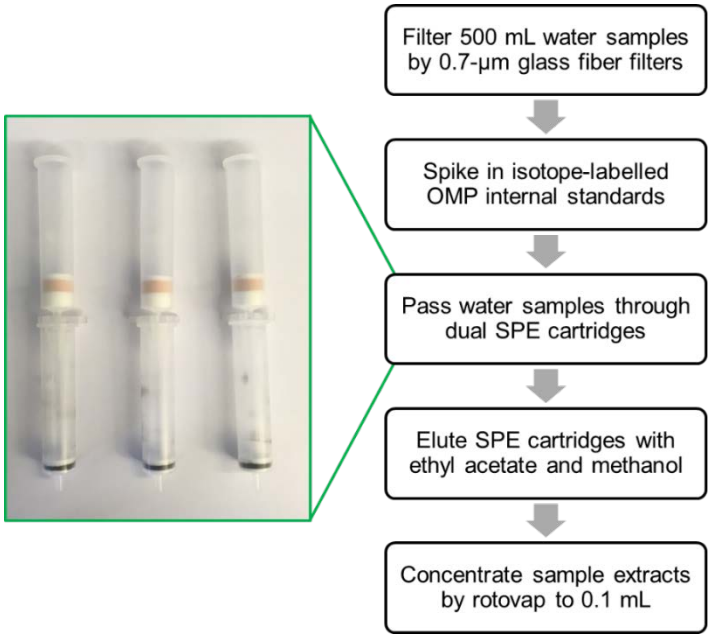

Figure 3. The general workflow for solid-phase extraction of water samples. Photo showing the dual SPE cartridges with the mixed-mode on top and single-mode at bottom.

2.2.2 Instrumental Analysis

Following SPE, chromatographic separation and mass spectrometric analysis were performed using a Dionex UltiMate 3000 high performance liquid chromatograph interfaced with a Thermo LTQ XL ion trap-Orbitrap high resolution mass spectrometer. Twenty µL of sample extracts was injected and separated on a Hypersil GOLD C18 column (100 × 2.1 mm, 1.9 µm; Thermo Scientific) equipped with a guard column. LC-MS grade water and methanol (both acidified with 0.1% v/v formic acid) were used as the mobile phases. The following gradient was applied for chromatographic separation: 90% water:10% methanol at 0 min, to 90% water:10% methanol at 4 min, to 5% water:95% methanol at 17 min, then held until 25 min, and back to 90% water:10% methanol from 25.1 to 29 min, at a flow rate of 200 µL/min and a column temperature of 30 °C. For the initial screening of mass spectral features, the full scan mass

spectra were acquired from 100 to 1500 Da with a nominal mass resolving power of 60,000 using positive and negative electrospray ionization in separate runs. For the structural elucidation of suspect hits, the data-dependent tandem mass spectra (i.e., MS/MS spectra) were acquired with a nominal mass resolving power of 7,500 using higher energy collision-induced dissociation (HCD). Normalized collision energies for HCD were set between 15 and 90, depending on the mass ranges of suspect hits. For the final confirmation of suspect hits, authentic reference standards were analyzed under similar conditions as described above to verify the retention times and MS/MS fragmentation patterns. Once confirmed with the standards, the concentrations of OMPs were quantified using 7-point calibration curves with reference to the isotope-labeled internal standards. For OMPs for which no structurally identical internal standards were available, the internal standards with the most similar retention times were used for quantification.

2.3 Suspect Screening Workflow Development

Following the analysis of sample extracts on LC-HRMS, raw MS data were processed for prioritization of OMPs that potentially occurred in the samples. Peak picking from the full scan MS spectra of samples was conducted using TraceFinder 4.1 (Thermo Scientific) following a set of predefined peak filtering criteria (e.g., area noise factor, peak noise factor, baseline window, peak area threshold, signal-to-noise ratio) according to previous studies.[63] Suspect database matching was conducted by comparing the accurate masses of picked peaks with the theoretical exact masses of the $[M + H]^+$ and $[M - H]^-$ adducts of compounds in an in-house suspect database with a mass tolerance of 5 ppm and isotopic pattern matching score of >65%. An initial suspect database was compiled from compounds in the following sources: U.S. FDA Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, U.S. FDA Green

Book: Approved Animal Drug Products, U.S. FDA High-Intensity Sweeteners, USEPA Pesticides Chemical Search, U.S. DEA Drugs of Abuse, Cosmetic Ingredient Review, USGS Techniques and Methods 5–B9 and 5–B11, USEPA Methods 1698, 544, and 545, and peer-reviewed journal articles that reported the occurrence of OMPs in New York State. Compounds with one or more of the following properties were excluded from the suspect database: (1) has an exact mass less than 100 Da or greater than 1500 Da, (2) contains only carbon and hydrogen atoms but no heteroatoms, or (3) contains a metallic element. The final suspect database included compound-specific information (e.g., CAS number, PubChem ID, IUPAC name, SMILES notation, molecular formula, exact mass, predicted Log*P*) for 2244 OMPs.

Suspect hits identified based on the database matching were subject to data-dependent MS/MS fragmentation using different HCD energies. The experimental MS/MS spectra were processed using Compound Discoverer 2.1 (Thermo Scientific) and searched through the online mass spectral database mzCloud (Thermo Scientific) or compared with *in silico* mass spectra predicted by Mass Frontier (HighChem). Mass spectral library search is by far the most efficient and reliable approach for compound identification. Matching experimental MS/MS spectra to those recorded from reference material provides a "match score" that measures the likelihood of a search spectrum corresponding to a reference spectrum in the library. For this study, mzCloud, a highly curated database that contains multistage MS spectral trees for over 8,000 compounds (as of July 5, 2018), was used for spectral library searches when possible. One critical challenge associated with the spectral library search, however, is that the availability of instrument-specific reference spectra in any given library is oftentimes limited. As a complementary tool to library search, *in silico* fragmentation performed by computational algorithms can predict theoretical MS/MS fragmentation patterns using bond dissociation or rule-based approaches.[65,68,73]

Matching experimental MS/MS spectra to those predicted by *in silico* fragment generation also yields a "match score" that is indicative of the similarity of spectra.[68] For this study, Mass Frontier, a commercial software that predicts MS/MS fragmentation based on literature reaction mechanisms, was used for *in silico* fragmentation.

To test the efficiency of spectral library search and *in silico* fragmentation for compound identification, two standard solutions containing low (25 ng/L) and high (750 ng/L) concentrations of 51 OMPs were extracted and analyzed under the conditions used for real water samples. These OMPs were selected to serve as the artificial suspects because they cover a range of Log*P*, pK_a, and structural features. The experimental MS/MS spectra of all 51 OMPs were matched with mass spectra currently available in mzCloud or those predicted by Mass Frontier. Overall, the mzCloud match scores for 51 OMPs ranged from 30 to 100, whereas the Mass Frontier match scores varied from 0 to 96.15. The efficiency of mzCloud library search for compound identification was calculated by dividing the number of OMPs with the mzCloud match scores above a certain threshold value by the total number of OMPs of interest (i.e., 51 in this case). For the 51 OMPs investigated, the efficiency dropped abruptly once the match score exceeded 90 (as shown in Figure 4), which corresponded to an efficiency of 88% and 94% for low (25 ng/L) and high (750 ng/L) OMP concentrations, respectively. Based on this analysis, an mzCloud match score of 90 was selected as the threshold to prioritize suspect hits for final confirmation. On the other hand, the Mass Frontier match scores failed to yield satisfactory efficiency for compound identification, as other previous studies have suggested.[63,82] Only a match score of 10 or lower yielded an efficiency of 90%. Mass Frontier relies on the rule-based fragmentation approach, which is known to work better with mass spectra generated by the more conventional ionization (e.g., electron ionization) and/or fragmentation (e.g., collision-induced

dissociation) techniques[83], but has limited utility for predicting spectra generated by alternative techniques (e.g., electrospray ionization and HCD) used in this study.

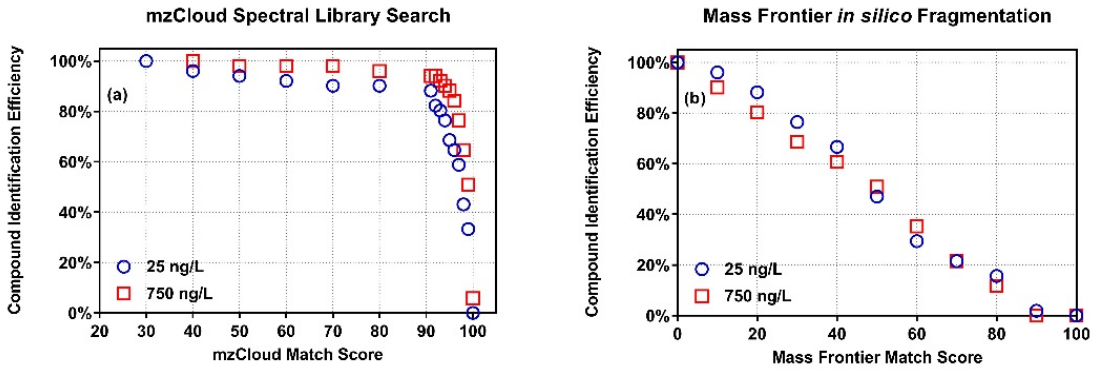

Figure 4. Plot of compound identification efficiency versus match score based on (a) mzCloud spectral library search and (b) Mass Frontier in silico fragmentation.

Suspect hits in water samples were prioritized following the screening workflow described above. The levels of confidence for suspect hits were assigned according to the criteria suggested by Schymanski et al.[65,84] Briefly, Level 1 (*confirmed structure*) indicates that the structure of suspect hit has been confirmed by measurements of an authentic reference standard. Level 2 (*probable structure*) indicates that the structure of suspect hit matches library reference spectra (Level 2a) or contains diagnostic MS/MS fragments (Level 2b). Level 3 (*tentative candidate(s)*) indicates that the suspect hit has tentative structures but insufficient information is available for unequivocal confirmation. In this study, suspect hits with mzCloud match scores above 90 were confirmed by reference standards and were assigned as Level 1. Suspect hits with mzCloud match scores above 30 but below 90 were assigned as Level 2, whereas those without mzCloud match scores were assigned as Level 3.

Chapter 3: Results and Discussion

3.1 Occurrence of OMPs in Onondaga Lake

Using the suspect screening workflow developed in this study, a total of 52 OMPs were prioritized and confirmed in the water samples collected from Onondaga Lake over the 5-month sampling period, as detailed in Table 2.

Table 2. Names and subcategories of OMPs detected in Onondaga Lake

Compound	**Subcategory**	**Compound**	**Subcategory**
Pharmaceuticals and TPs (PHAR)		Ritalinic acid	TP of Methylphenidate
Levetiracetam*	Anticonvulsant	Desvenlafaxine	TP of Venlafaxine
Gabapentin*	Anticonvulsant	Benzoylecgonine	TP of Cocaine
Lamotrigine*	Anticonvulsant	N4-Acetylsulfamethoxazole	TP of Sulfamethoxazole
Carbamazepine*	Anticonvulsant	Cotinine	TP of Nicotine
Phenytoin	Anticonvulsant	**Household/Industrial Chemicals and TPs (HHIND)**	
Venlafaxine	Antidepressant	Benzotriazole*	Corrosion inhibitor
Fexofenadine	Antihistamine	Methyl benzotriazole*	Corrosion inhibitor
Cetirizine*	Antihistamine	Benzothiazole	Corrosion inhibitor
Sulfamethoxazole*	Antibiotic	Benzophenone	UV filter
Trimethoprim*	Antibiotic	Oxybenzone	UV filter
Losartan*	Antihypertensive	Tris(2-chloroethyl) phosphate	Flame retardant
Irbesartan*	Antihypertensive	Melamine	Plasticizer
Valsartan	Antihypertensive	Sucralose*	Artificial sweetener
Estradiol*	Steroid hormone	Caffeine	Food additive
Dihydrotestosterone	Steroid hormone	DEET	Insect repellent
Androstenedione	Steroid hormone	Galaxolidone*	TP of Galaxolide
Lidocaine*	Antiarrhythmic	**Pesticides and TPs (PEST)**	
Naproxen	Analgesic	Atrazine*	Herbicide
Atenolol	Antihypertensive	Metolachlor*	Herbicide
Metoprolol	Antihypertensive	Prometon*	Herbicide
Metaxalone*	Muscle relaxant	2,4-D	Herbicide
Methocarbamol	Muscle relaxant	Diuron*	Herbicide
Fluconazole*	Antifungal	Propazine	Herbicide
Metformin*	Antidiabetic	Atrazine-desisopropyl*	TP of Atrazine
Amantadine*	Antiviral	Atrazine-2-hydroxy*	TP of Atrazine
Gemfibrozil*	Anticoagulant	Atrazine-desethyl*	TP of Atrazine
Dopamine*	Neurotransmitter	*Detected in 100% of the lake samples	

Among the 52 OMPs, 32 can be broadly classified as pharmaceuticals and their TPs (hereafter referred to as the "PHAR" category), 11 as household/industrial chemicals and their TPs (hereafter referred to as the "HHIND" category), and 9 as pesticides and their TPs (hereafter referred to as the "PEST" category). Twenty-eight of the 52 OMPs were detected in 100% of the samples, most of which are synthetic bioactive chemicals such as pharmaceuticals and pesticides. Generally, the spectrum of OMPs found in Onondaga Lake is similar to those reported for surface waters with known wastewater influence and/or recreational usage. For example, gabapentin, gemfibrozil, sulfamethoxazole, trimethoprim, carbamazepine, benzotriazole, methyl benzotriazole, sucralose, and atrazine detected in 100% of the lake water samples were also the most frequently found OMPs Lake Geneva[85] and Lake Constance[86] in Europe.

Overall, concentrations of individual OMPs varied by 3 orders of magnitude from <2 ng/L up to >7,000 ng/L across sites L1-L4 in Onondaga Lake, as shown in Figure 5. Summed concentrations of detected OMPs ranged from 3,025 to 13,750 ng/L per site. Sucralose, an artificial sweetener sold under the trade name Splenda®, occurred at the highest concentration (1,180-7,060 ng/L across sites L1-L4) among all OMPs detected. Sucralose is a chlorinated form of sucrose that is highly stable and can hardly be removed by mechanical-biological wastewater treatment processes.[87–89] Earlier studies reporting the occurrence of sucralose in environmental waters were mainly conducted in European countries[90,91], where the concentration of sucralose was typically below 1,000 ng/L. Sucralose was later measured in the U.S. coastal waters, wastewater-impacted rivers, and alluvial groundwater.[92–95] A 2016 national reconnaissance reported a mean concentration of sucralose (1,340 ng/L) in surface waters of 37 lotic ecosystems in the U.S. Furthermore, sucralose occurrence was recently reported in the Hudson River Estuary and the New York Harbor[14,15] with concentrations reaching up to low μg/L levels. Because of its

persistence and mobility, sucralose was proposed as a conservative indicator compound[95] for wastewater loading in surface waters and its concentration has been suggested to serve as a good predictor of summed concentrations and/or detection frequencies[14,96] of other OMPs detected in surface waters. Indeed, the concentration of sucralose was found to have a strong, positive correlation with the summed concentration of OMPs (R^2 = 0.82; p <0.0001) in Onondaga Lake.

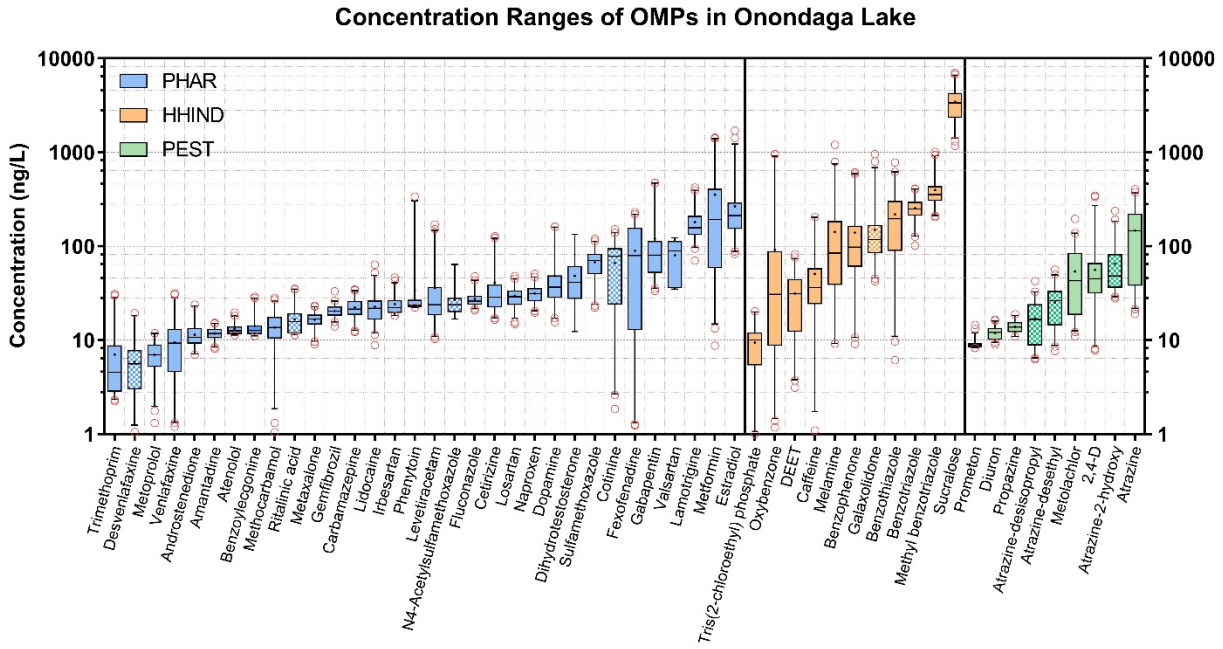

Figure 5. Concentration ranges of OMPs detected at sites L1-L4 in Onondaga Lake during June and October 2017. “PHAR” refers to pharmaceuticals and their transformation products. “HHIND” refers to household/industrial chemicals and their transformation products. “PEST” refers to pesticides and their transformation products. For each category, individual OMPs were plotted with increasing median concentrations from left to right. Transformation products were labeled using the diagonal stripe pattern. The box represents the 0.025 and 0.975 percentiles. The whiskers mark the last value within a range of 1.5 times the 0.025 and 0.975 percentiles. The bar within the box represents the median. The “+” symbol represents the mean. The red circles denote the outliers.

Corrosion inhibitors, such as benzotriazole, methyl benzotriazole, and benzothiazole, also frequently occurred at high concentrations in Onondaga Lake. The concentrations of benzotriazole, methyl benzotriazole, and benzothiazole ranged from 102-411 ng/L, 205-1,015 ng/L, and 6-781 ng/L, respectively, across sites L1-L4. Both benzotriazoles and benzothiazoles

are high production volume heterocyclic aromatic compounds used in a variety of consumer products and industrial applications. Several previous studies have reported the occurrence of these two groups of OMPs in European and U.S. surface waters.[97–101] For example, benzotriazole and methyl benzotriazole were detected in 12 Swiss rivers[101] with median concentrations of 1,000 and 200 ng/L, respectively, whereas benzotriazole was measured in Lake Greifensee, Lake Zurich, and Lake Geneva[101] at concentrations of 1,200, 100-400, and 200 ng/L, respectively. Benzothiazole was reported to occur in rivers within the Schwarzbach watershed in Germany at concentrations of 58-856 ng/L.[102] Methyl benzotriazole was detected in 17 of 54 samples from U.S. streams with the maximum and median concentrations of 2,400 and 390 ng/L, respectively.[38]

Besides sucralose and corrosion inhibitors, three pharmaceuticals, metformin, estradiol, lamotrigine, and one pesticide, atrazine, also occurred at relatively high levels in Onondaga Lake, with a mean concentration of 355, 266, 181, and 147 ng/L, respectively. Metformin is one of most prescribed pharmaceuticals by mass worldwide and has been detected in streams across U.S.[13] with median concentrations greater than 400 ng/L as well as in wastewater-impacted European rivers[103–105] in the range of 1,000-3,000 ng/L. Estradiol is a steroidal estrogen hormone that has been detected at low concentrations in the range of ng/L to µg/L in streams[38,106] and ponds receiving agricultural wastewater,[107] in runoff from fields following land application of animal waste,[108] in streams draining livestock farms[109] and rangeland,[110] and in groundwater within intensively farmed agricultural areas.[107] Lamotrigine is an anticonvulsant used in combination with carbamazepine for a wide range of seizure disorders in children and adults and has been detected in surface and groundwaters sampled from 9 U.S. states[111] at a mean concentration of 108 and 324 ng/L, respectively. Atrazine is one of the most widely used

herbicides with approximately 80 million pounds applied annually in the U.S. alone and has been frequently detected in U.S. surface and groundwaters, particularly in the Midwest, where it is heavily used on corn.[33] The majority of other OMPs occurred at concentrations between 1 and 100 ng/L, which is typical of levels reported for other surface water systems in the U.S.

Temporal variations in summed concentration profiles of three major categories of OMPs were illustrated in Figure 6. For OMPs belonging to the PHAR and HHIND categories, the mean summed concentration appeared to decrease from late June to early August but increase thereafter. In contrast, for OMPs belonging to the PEST category, the mean summed concentration gradually decreased from June to October, despite some fluctuations between late June and July. Differences in temporal trends for OMPs may reflect differences in their consumption patterns (e.g., higher application rates of pesticides during summer months) and physicochemical properties governing environmental fate and transport. However, additional analyses on sources and transport in the lake watershed, as well as detailed knowledge about the persistence and mobility of individual OMPs, are required to better interpret the trends observed.

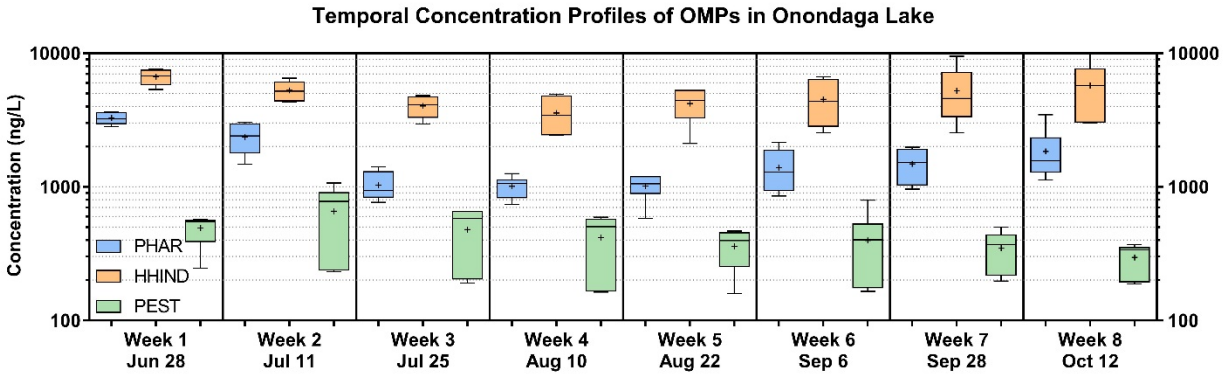

Figure 6. Temporal concentration profiles of three groups of OMPs at sites L1-L4 in Onondaga Lake during June and October 2017. "PHAR" refers to pharmaceuticals and their transformation products. "HHIND" refers to household/industrial chemicals and their transformation products. "PEST" refers to pesticides and their transformation products. The box represents the 0.025 and 0.975 percentiles. The whiskers mark the last value within a range of 1.5 times the 0.025 and

0.975 percentiles. The bar within the box represents the median. The "+" symbol represents the mean.

Horizontal variations in summed concentration profiles of three major categories of OMPs were illustrated in Figure 7. For OMPs belonging to the PHAR and HHIND categories, the mean summed concentration slightly decreased from site L1 (closest to the WWTP which is located at the southern end of the lake) to L4 (furthest from the WWTP), which is expected assuming that these OMPs were mainly contributed by wastewater effluent discharged into the lake at the southern end. On the other hand, the mean summed concentration for OMPs belonging to the PEST category did not exhibit significant changes from site L1 to L4. For all three categories of OMPs, the mean summed concentration in the epilimnion was somewhat higher than that in the hypolimnion, suggesting variations in the vertical distribution of OMPs in the lake water column.

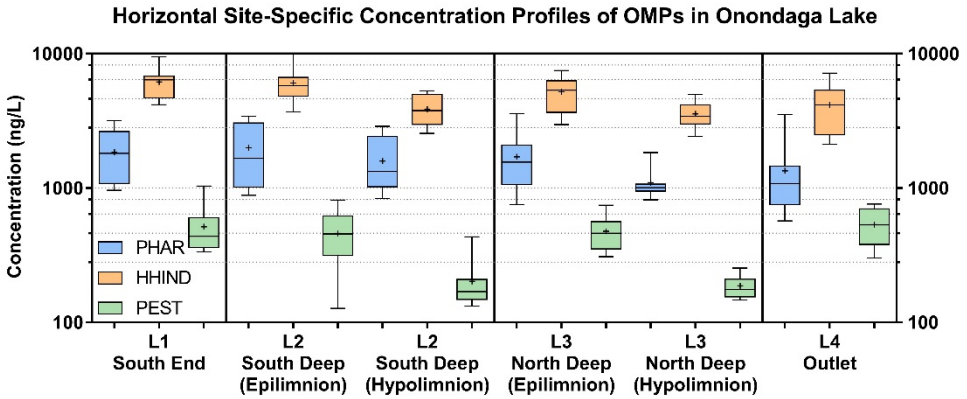

Figure 7. Horizontal concentration profiles of three groups of OMPs across sites L1-L4 in Onondaga Lake during June and October 2017. "PHAR" refers to pharmaceuticals and their transformation products. "HHIND" refers to household/industrial chemicals and their transformation products. "PEST" refers to pesticides and their transformation products. The box represents the 0.025 and 0.975 percentiles. The whiskers mark the last value within a range of 1.5 times the 0.025 and 0.975 percentiles. The bar within the box represents the median. The "+" symbol represents the mean. Note that samples at sites L2 and L3 were collected from two different depths, with one from epilimnion and the other from hypolimnion.

Onondaga Lake is thermally stratified into between late May and late October.[75] To further investigate the potential impacts of stratification on OMP distribution in the water column, two

sets of depth profile samples were collected at site L2 for OMP analysis. As shown by the temperature and dissolved oxygen profiles in Figure 8, the lake was stratified into three layers in early July 2017, with the warm water epilimnion and the cold water hypolimnion separated by a thermocline layer formed between 6 and 8 m depth. Generally, the discharge of wastewater effluent into Onondaga Lake was evident from the depth profile of specific conductance, as shown in Figure 8. The sharp spike in specific conductance at 7 m depth, possibly arising from elevated salinity contributed by wastewater effluent, indicated the possible presence of a wastewater plume in the thermocline. The lake remained stratified in early October 2017, but the thermocline layer shifted downwards to between 9 and 12 m depth, presumably allowing mixing of discharged wastewater in the epilimnion. Furthermore, the specific conductance in the epilimnion was higher than that in the hypolimnion, which was different than the case in early July 2017. Indeed, previous research conducted by the UFI has shown that the WWTP effluent is typically cooler (negatively buoyant) relative to the water of the epilimnion from late spring to late summer, and warmer (positively buoyant) thereafter through fall.[7,112] Thus, the wastewater effluent is typically observed as interflow (into the thermocline) and overflow (over the thermocline) patterns in summer and fall, respectively.

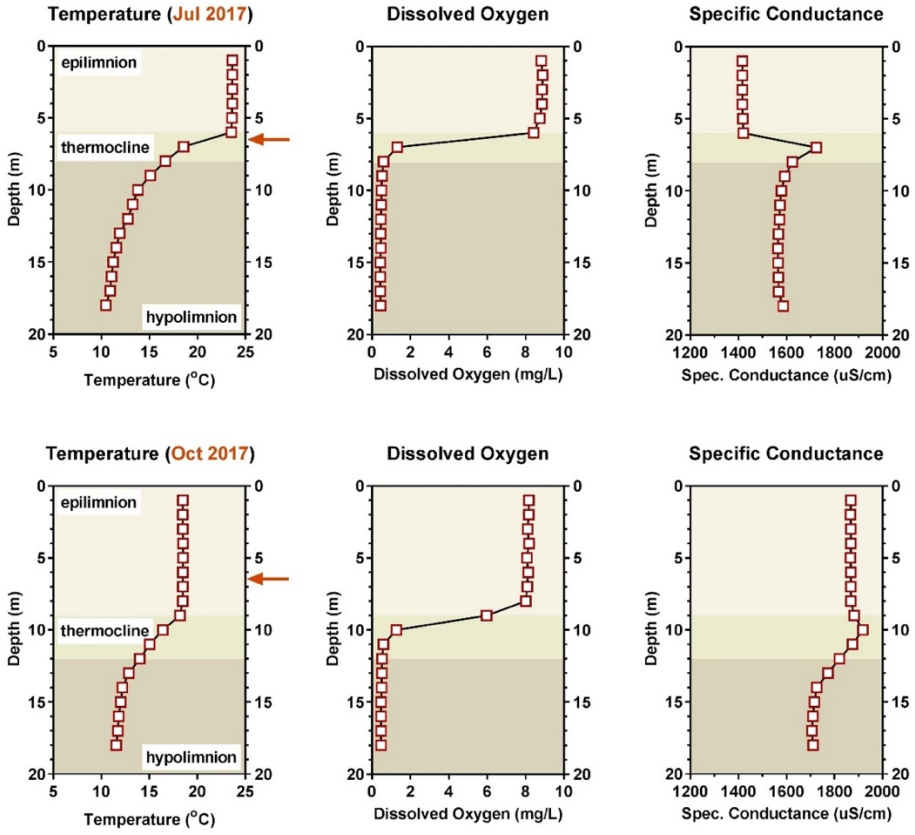

Figure 8. Depth profiles of temperature, dissolved oxygen, and specific conductance at site L2 in July and October 2017, respectively. The boundaries of epilimnion, thermocline, and hypolimnion were defined based on the temperature profiles. The orange arrow indicates the hypothetical entry depth of the WWTP effluent based on previous literature.

Given that OMPs present in Onondaga Lake may originate from different sources, their depth concentration profiles would likely exhibit different patterns. To test this hypothesis, a principal component analysis (PCA) was performed with R 3.5.3 using the package "FactoMineR". Concentrations of individual OMPs measured in all lake samples were used as inputs for the PCA. As shown in Figure 9, two principal components together explained 63.9% of the variance in the OMP concentration data, highlighting two major groups of OMPs. The first group of OMPs were located towards the positive end of the *x*-axis with high PC1 loadings and low-to-moderate PC2 loadings. The second group of OMPs were located towards the positive end of *y*-axis with low PC1 loadings but moderate-to-high PC2 loadings. Closer examination of

the first group of OMPs revealed that most of them belonged to the PHAR and HHIND categories and were most likely derived from point sources such as urban wastewater discharge, while the second group of OMPs mainly belonged to the PEST category and were most likely associated with agriculture-derived diffuse runoff, with a few exceptions (i.e., oxybenzone, caffeine, cotinine). Oxybenzone is a UV filter used in sunscreen products, caffeine is a stimulant, and cotinine is a metabolite of nicotine, all of which are lifestyle chemicals that have been frequently detected in urban runoff (e.g., combined sewer overflows), but also in agricultural settings (e.g., the application of biosolids).[11,28,47]

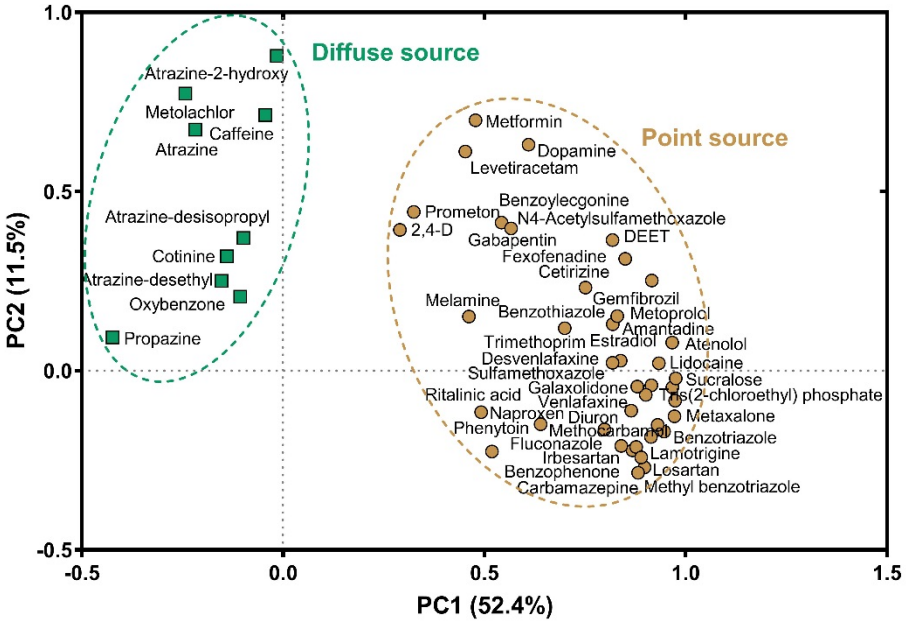

Figure 9. Component plot showing the grouping of OMPs in Onondaga Lake based on the principal component (PC) loadings of individual OMPs.

Grouping OMPs based the PCA results yielded two distinct types of depth concentration profiles for OMPs, as shown in Figure 10. In early July 2017, OMPs originating from point-source wastewater exhibited peak concentrations in the thermocline, most likely due to the discharge of wastewater effluent from the WWTP. Meanwhile, OMPs originating from diffuse sources did not exhibit such feature, suggesting that these OMPs mainly entered Onondaga Lake

from land or tributaries, but not via wastewater discharge. Given that site L2 is located ~3 km away from the WWTP shoreline outfall, the observed plume of OMPs implied a horizontal extension from the outfall to L2, although tracer tests would be required to verify the extent of horizontal spreading. In early October 2017, the plume phenomenon for OMPs originating from point-source wastewater discharge disappeared and could be explained by the mixing of wastewater effluent that created a more homogenous concentration profile in the epilimnion. On average, the concentrations of point-source OMPs measured in early October 2017 were higher than those measured in early July 2017, whereas the opposite was true for diffuse-source OMPs. This observation is in line with results from the horizontal site-specific measurements discussed above. Prior work by Bonvin et al. 2011 reported a similar wastewater plume phenomenon in Lake Geneva, Switzerland, where wastewater effluent discharged into the lake at ~30 m depth (i.e., hypolimnion) was trapped below the warmer epilimnion from April to August, resulting in concentration peaks of 21 pharmaceuticals below the epilimnion.[85] Similarly, Schimmelpfennig et al. 2016 also reported the impacts of seasonal variations in the density stratification on the vertical distribution of 3 pharmaceuticals in Lake Tegel, Germany.[113]

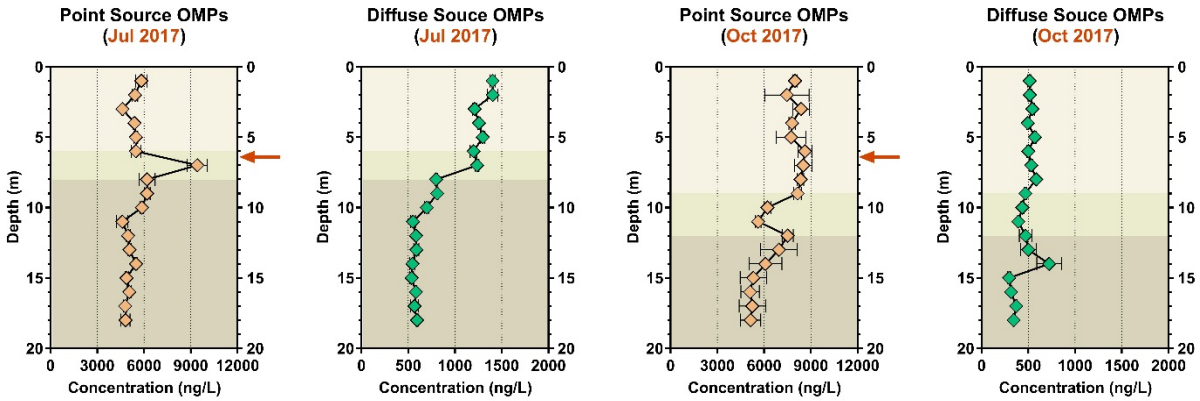

Figure 10. Depth concentration profiles of OMPs at site L2 in July and October 2017, respectively. The boundaries of epilimnion, thermocline, and hypolimnion were defined based on the temperature profiles. The orange arrow indicates the hypothetical entry depth of the WWTP effluent based on previous literature.

3.2 Occurrence of OMPs in Lake Tributaries

Compared to Onondaga Lake, fewer OMPs were detected in the water samples collected from the four tributaries (i.e., T1-T4) of Onondaga Lake. A total of 31 OMPs were confirmed and quantified, of which 12 belonged to the PHAR category, 10 belonged to the HHIND category, and 8 belonged to the PEST category, as listed in Table 3.

Table 3. Names and subcategories of OMPs detected in the four lake tributaries

Compound	**Subcategory**	**Compound**	**Subcategory**
Pharmaceuticals and TPs (PHAR)		Benzophenone	UV filter
Levetiracetam	Anticonvulsant	Oxybenzone*	UV filter
Gabapentin	Anticonvulsant	Tris(2-chloroethyl) phosphate	Flame retardant
Lamotrigine*	Anticonvulsant	Melamine	Plasticizer
Fexofenadine	Antihistamine	Sucralose*	Artificial sweetener
Estradiol*	Steroid hormone	DEET	Insect repellent
Dihydrotestosterone	Steroid hormone	Galaxolidone	TP of Galaxolide
Naproxen	Analgesic	**Pesticides and TPs (PEST)**	
Metformin	Antidiabetic	Atrazine*	Herbicide
Gemfibrozil	Anticoagulant	Metolachlor	Herbicide
Dopamine	Neurotransmitter	Prometon	Herbicide
Ritalinic acid	TP of Methylphenidate	2,4-D	Herbicide
Cotinine	TP of Nicotine	Diuron	Herbicide
Household/Industrial Chemicals and TPs (HHIND)		Propazine	Herbicide
Benzotriazole*	Corrosion inhibitor	Atrazine-desisopropyl*	TP of Atrazine
Methyl benzotriazole*	Corrosion inhibitor	Atrazine-2-hydroxy*	TP of Atrazine
Benzothiazole	Corrosion inhibitor	Atrazine-desethyl*	TP of Atrazine
		*Detected in 100% of the tributary samples	

Ten of the 31 OMPs were detected in 100% of the tributary samples. Among these, lamotrigine, estradiol, benzotriazole, methyl benzotriazole, sucralose, atrazine, and the three atrazine TPs were also detected in all the lake samples, indicating the ubiquitous presence of these OMPs in the lake watershed. The fact that sucralose was detected in all the tributary samples suggests that the tributaries also received wastewater inputs, though no major wastewater treatment plant directly discharges effluents into these tributaries. Indeed, previous studies have reported that the tributaries receive discharges of raw wastewater via combined

sewer overflows during runoff events[114] or inputs of raw wastewater via sewer leaks,[115] which serve as potential sources of OMPs. Concentrations of most OMPs fell between 10-100 ng/L across tributaries T1-T4, as shown in Figure 11. Generally, these concentrations were lower or comparable to those measured in Onondaga Lake, which was expected given that the lake directly receives a relatively high percentage of wastewater inflow.

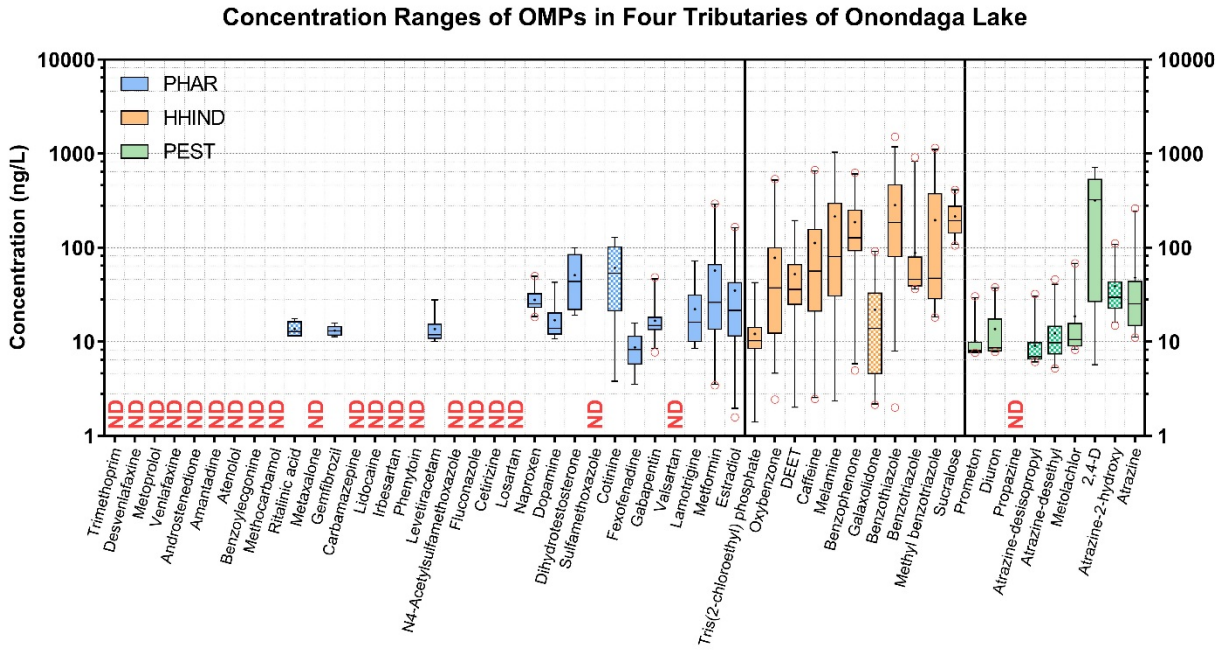

Figure 11. Concentration ranges of OMPs detected at sites T1-T4 during June and October 2017. "PHAR" refers to pharmaceuticals and their transformation products. "HHIND" refers to household/industrial chemicals and their transformation products. "PEST" refers to pesticides and their transformation products. For comparison purpose, individual OMPs were plotted from left to right following the same order as shown in Figure 5. Transformation products were labeled using the diagonal stripe pattern. The box represents the 0.025 and 0.975 percentiles. The whiskers mark the last value within a range of 1.5 times the 0.025 and 0.975 percentiles. The bar within the box represents the median. The "+" symbol represents the mean. The red circles denote the outliers. "ND" indicates that the OMP was not detected in the tributary samples.

The summed concentrations of OMPs were on the same order of magnitude with some variability in individual categories for different tributaries, as shown in Figure 12. For instance, tributary T4 (Ley Creek) had the highest summed concentrations of OMPs belonging to the PHAR and HHIND categories, while tributary T2 (Onondaga Creek) showed the lowest summed

concentrations of these two categories of OMPs. Further examination of the land use characteristics of tributary sub-watersheds (Table 4) revealed that both agricultural and urban are important land use types, which provides some context for the occurrence of OMPs in these tributaries. However, no significant correlations were identified between the percent agricultural or urban land use in the sub-watersheds and the summed concentration of OMPs in the tributaries. Several recent studies have combined geospatial analysis and statistical tools to identify the relative contributions of various sources of OMPs at the watershed scale.[11,15,40,59] Further work is needed to explore the utility of these tools and long-term monitoring data for source appointment of OMPs in the Onondaga Lake watershed.

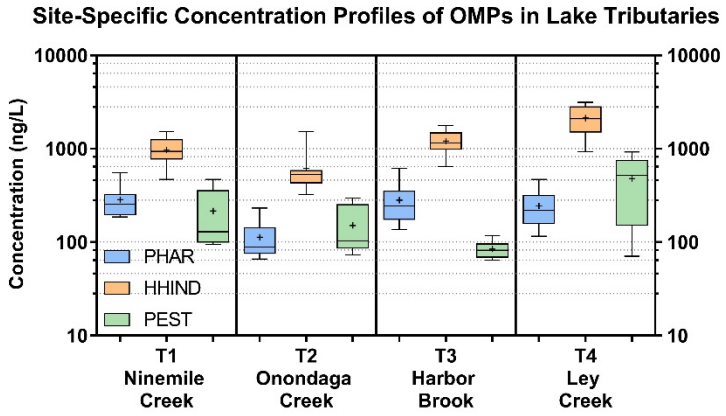

Figure 12. Concentration profiles of three groups of OMPs in tributaries T1-T4 during June and October 2017. "PHAR" refers to pharmaceuticals and their transformation products. "HHIND" refers to household/industrial chemicals and their transformation products. "PEST" refers to pesticides and their transformation products. The box represents the 0.025 and 0.975 percentiles. The whiskers mark the last value within a range of 1.5 times the 0.025 and 0.975 percentiles. The bar within the box represents the median. The "+" symbol represents the mean.

Table 4. Characteristics of Onondaga Lake watershed land use

Tributary	Drainage area		Percent cover by land use type			
	Area (km^2)	Percent of total	Forest	Agricultural	Urban	Other
T1 (Ninemile Creek)	298	41	41	40	7	12
T2 (Onondaga Creek)	285	39	50	31	12	7
T3 (Harbor Brook)	35	5	28	22	41	9
T4 (Ley Creek)	76	10	18	8	55	19
"Other" includes wetlands, open water, and grasses; Land us data in the table taken from Rhea et al. (2006)[116]						

3.3 Occurrence of OMPs in the Seneca-Oneida-Oswego River System

A total of 37 OMPs were quantified in the water samples collected from the Seneca-Oneida-Oswego River (i.e., Three Rivers) system, as shown in Table 5.

Table 5. Names and subcategories of OMPs detected in the Three Rivers

Compound	**Subcategory**	**Compound**	**Subcategory**
Pharmaceuticals and TPs (PHAR)		**Household/Industrial Chemicals and TPs (HHIND)**	
Levetiracetam*	Anticonvulsant	Benzotriazole*	Corrosion inhibitor
Gabapentin*	Anticonvulsant	Methyl benzotriazole*	Corrosion inhibitor
Lamotrigine*	Anticonvulsant	Benzothiazole*	Corrosion inhibitor
Carbamazepine*	Anticonvulsant	Benzophenone*	UV filter
Fexofenadine*	Antihistamine	Oxybenzone*	UV filter
Cetirizine*	Antihistamine	Tris(2-chloroethyl) phosphate*	Flame retardant
Sulfamethoxazole	Antibiotic	Melamine	Plasticizer
Losartan*	Antihypertensive	Sucralose*	Artificial sweetener
Irbesartan*	Antihypertensive	Caffeine*	Food additive
Estradiol*	Steroid hormone	DEET	Insect repellent
Lidocaine*	Antiarrhythmic	Galaxolidone*	TP of Galaxolide
Naproxen*	Analgesic	**Pesticides and TPs (PEST)**	
Metaxalone*	Muscle relaxant	Atrazine*	Herbicide
Methocarbamol*	Muscle relaxant	Metolachlor*	Herbicide
Fluconazole*	Antifungal	2,4-D	Herbicide
Metformin*	Antidiabetic	Propazine*	Herbicide
Gemfibrozil*	Anticoagulant	Atrazine-desisopropyl*	TP of Atrazine
Ritalinic acid*	TP of Methylphenidate	Atrazine-2-hydroxy*	TP of Atrazine
Cotinine	TP of Nicotine	Atrazine-desethyl*	TP of Atrazine
		*Detected in 100% of the river samples	

Thirty-two of the 37 OMPs were detected in 100% of the river samples. Concentrations of most OMPs belonging to the PHAR and PEST categories ranged from 10-100 ng/L, while concentrations of OMPs belonging to the HHIND category varied from <10 to >1000 ng/L, as shown in Figure 13. Similar to the findings with Onondaga Lake and its tributaries, six OMPs, including lamotrigine, estradiol, benzotriazole, methyl benzotriazole, sucralose, and atrazine, also occurred at relatively high concentrations with 100% detection frequency in the Three Rivers. While previous nationwide or regional studies[13,15] have identified some other specific

compounds as predictors of overall OMP occurrence, this core cluster of OMPs can potentially serve as indicator compounds in the Onondaga Lake-Three Rivers system.

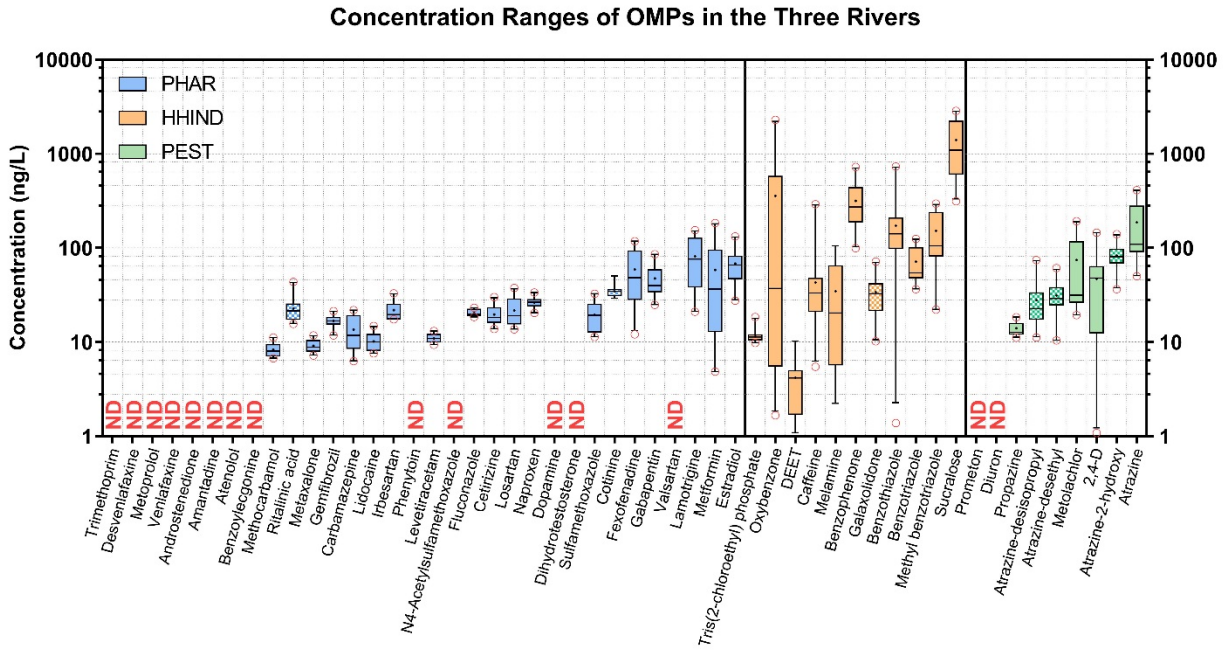

Figure 13. Concentration ranges of OMPs detected in the Three Rivers during June and October 2017. "PHAR" refers to pharmaceuticals and their transformation products. "HHIND" refers to household/industrial chemicals and their transformation products. "PEST" refers to pesticides and their transformation products. For comparison purpose, individual OMPs were plotted from left to right following the same order as shown in Figure 5. Transformation products were labeled using the diagonal stripe pattern. The box represents the 0.025 and 0.975 percentiles. The whiskers mark the last value within a range of 1.5 times the 0.025 and 0.975 percentiles. The bar within the box represents the median. The "+" symbol represents the mean. The red circles denote the outliers. "ND" indicates that the OMP was not detected in the river samples.

As shown in Figure 14, the longitudinal concentration profiles of OMPs in the Three Rivers were relatively consistent in July and October 2017, suggesting a steady input of OMPs into the system. The summed concentrations of OMPs belonging to the PHAR and HHIND categories were generally higher in October than in July, while the opposite was true for OMPs belonging to the PEST category, concurring with the trends seen for Onondaga Lake.

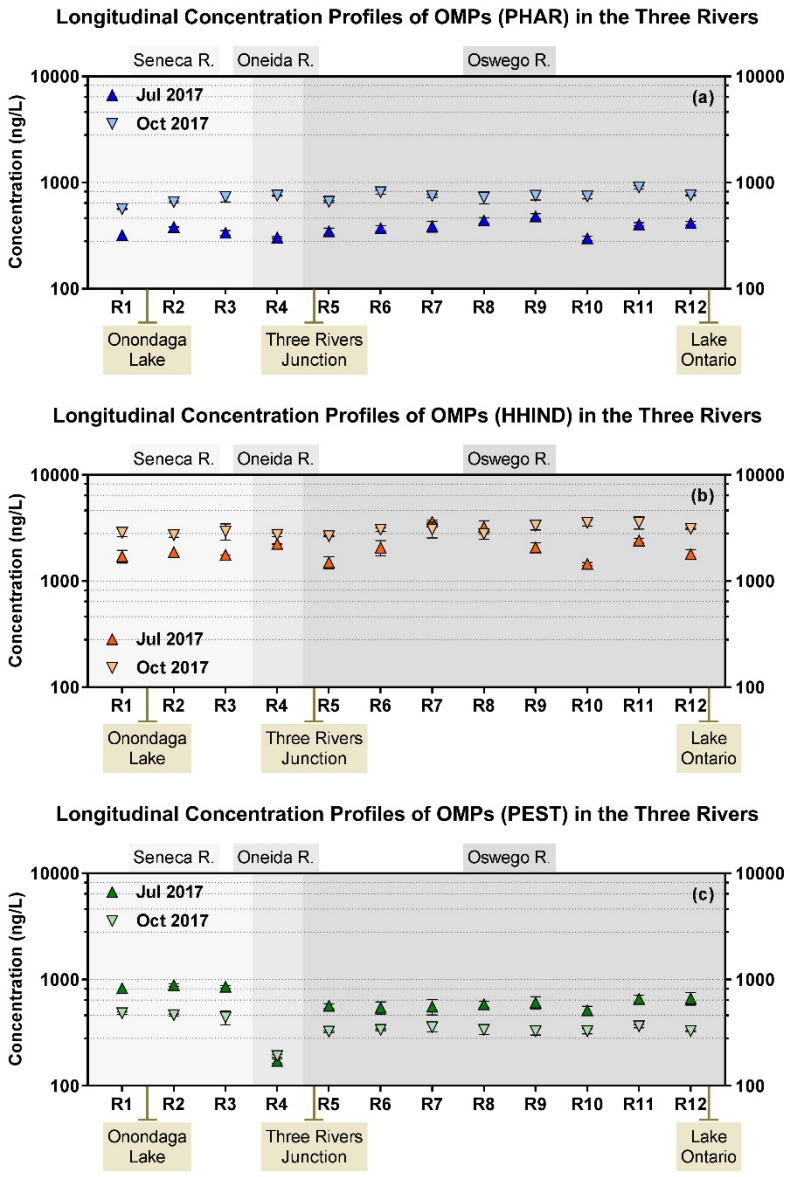

Figure 14. Longitudinal concentration profiles of OMPs in the Three Rivers during June and October 2017, respectively. “PHAR” refers to pharmaceuticals and their transformation products. “HHIND” refers to household/industrial chemicals and their transformation products. “PEST” refers to pesticides and their transformation products.

3.4 Mass Flows of OMPs in the Lake-River System

To further evaluate the relative importance of OMP sources in the Onondaga Lake-Three Rivers system, the mass flows of OMPs in and out of Onondaga Lake and the Three Rivers were estimated using the measured OMP concentrations and flow rate data available from USGS and the WWTP. As discussed above, the WWTP and four tributaries represent the major hydrologic inputs into Onondaga Lake. Long-term flow rates for the four tributaries T1 (Ninemile Creek), T2 (Onondaga Creek), T3 (Harbor Brook), and T4 (Ley Creek) are monitored by USGS gauging stations (15-minute and daily-averaged) at the tributary mouths. Daily discharge flow rates for the WWTP are also available as required by the plant's discharge permit. The outflow rate of Onondaga Lake is not directly monitored but can be approximated by summing the flow rates of major inflows to the lake, an approach that has been successfully implemented for mass balance analyses and modeling for lake water quality in previous work. Furthermore, summing the estimated Onondaga Lake outflow rate and the Seneca River and Oneida River flow rates typically provides a reasonably good estimation of the Oswego River flow rate. Long-term flow rates for all three rivers are also monitored by USGS. A simplified schematic for the lake-river system is shown below (Figure 15) to help define flow and boundary conditions.

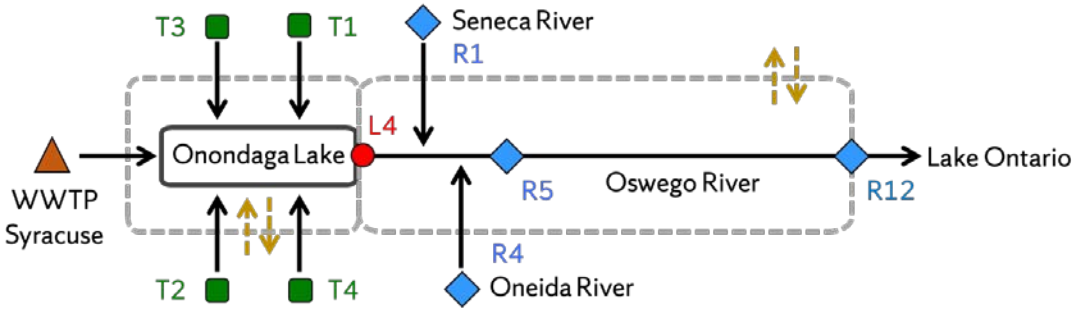

Figure 15. A simplified schematic showing the mass flows of OMPs in and out of the Onondaga Lake-Three Rivers system (not to scale). The dash boxes indicate the boundaries defined for mass balance analyses. The dash arrows represent unknown mass flows of OMPs that were not accounted for in this study.

For Onondaga Lake (Figure 16), the mass flows of OMPs contributed by tributaries were calculated by multiplying the concentrations of OMPs with the daily-averaged flow rates, assuming that the tributary water columns were well-mixed. The mass flow of OMPs exiting Onondaga Lake was estimated by multiplying the summed concentration of OMPs at site L4 (outlet) with the estimated outflow rate. Over the sampling period, wastewater inputs accounted for 28.5±5.7% of the total lake inflow (Table 6). For a conservative estimate, the mass flow of OMPs contributed by the WWTP could be approximated by subtracting the mass flows of tributaries off from that estimated at the lake outlet, assuming no other inputs of OMPs and no removal of OMPs after being released into Onondaga Lake. The percent contribution of a given inflow shown in Table 6 was calculated by dividing the mass flows of OMPs from that inflow to those estimated for the lake outflow. Using this approach, the WWTP mass flows of OMPs belonging to the PHAR and HHIND categories were estimated to account for up to 86% and 79%, respectively, of the total outlet mass flows (Table 6), highlighting the WWTP as a significant contributor of OMPs as compared to the lake tributaries. Furthermore, the WWTP also served as a dominant source of OMPs belonging to the PEST category and accounted for ~67% of the total outlet mass flow of these OMPs.

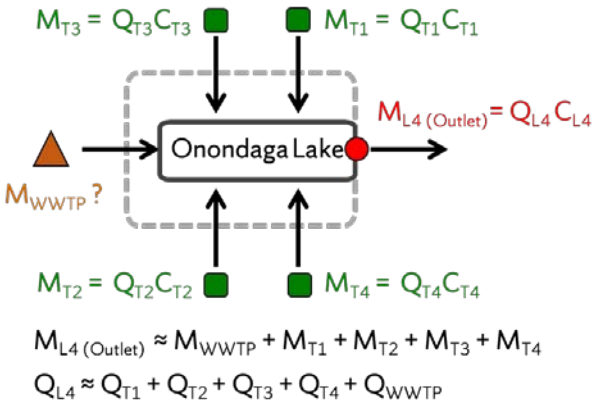

Figure 16. A simplified schematic showing the mass flows of OMPs in and out of Onondaga Lake (not to scale), where "M" = mass flow, "Q" = flow rate, and "C" = OMP concentration. The dash box indicates the boundary for mass flow analysis.

Table 6. Percent contributions of OMP mass flows in Onondaga Lake

	PHAR (%)	**HHIND (%)**	**PEST (%)**	**Flow (%)**
T1 (Ninemile Creek)	7.8±2.8	8.8±4.9	13.2±8.5	31.9±4.5
T2 (Onondaga Creek)	2.9±1.7	5.4±5.5	8.0±4.4	28.1±4.1
T3 (Harbor Brook)	0.6±0.5	0.8±0.6	0.4±0.2	2.2±0.5
T4 (Ley Creek)	2.2±1.9	6.1±5.7	11.7±11.4	9.4±4.5
Syracuse WWTP	86.5±3.8	78.9±9.3	66.7±15.0	28.5±5.7

For the Three Rivers (Figure 17), the mass flows of OMPs in each river were calculated by multiplying the concentrations of OMPs at selected sites (i.e., site R1 for Seneca, site R4 for Oneida, and sites R5 and R12 for Oswego) measured in July and October 2017 with the daily-averaged flow rates, again assuming that the river water columns were well-mixed. The mass flows of OMPs exiting Onondaga Lake was estimated as described above with data from July and October 2017. The percent contribution of a given inflow shown in Table 7 was calculated by dividing the mass flows of OMPs from that inflow to those estimated for the Oswego River outflow at Lake Ontario. Based on this analysis, Onondaga Lake itself was found to contribute ~12-24% of OMPs to the lake-river system (Table 7), despite its relatively small outflow rate (10.8±4.7%) compared to the Seneca River and Oneida River. The Seneca River contributed the largest mass flows of OMPs, likely due to discharges from over 30 small WWTPs and

agricultural inputs within the Seneca River basin.[117,118] Similarly, the Oneida River and Oswego River (from the two river confluence to Lake Ontario entry) also served as important contributors of OMPs to the system. Summing all percent contributions from the lake and the rivers gave reasonable estimates (~100%) of the mass flows of three different categories of OMPs at the Oswego River mouth (i.e., prior to entry to Lake Ontario). This suggests that the mass flow analysis was acceptable given the uncertainties involved in the flow and concentration measurements as well as the unknown sources and sinks of OMPs that were not accounted for.

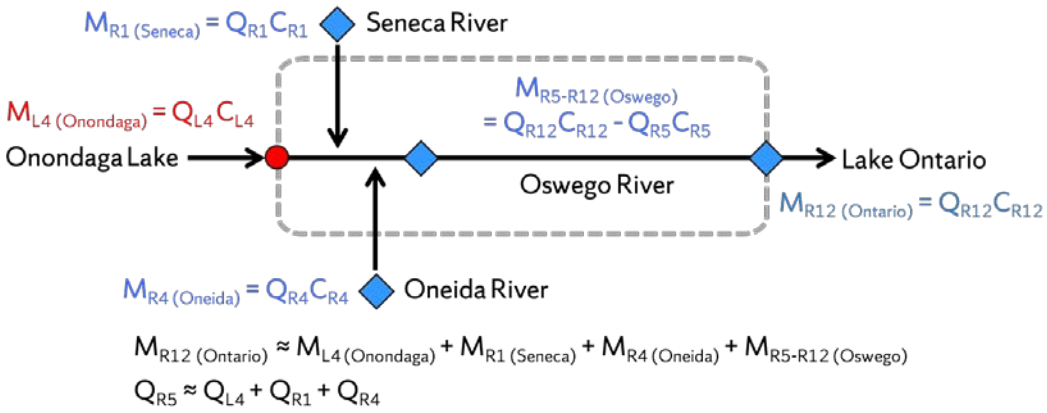

Figure 17. A simplified schematic showing the mass flows of OMPs in and out of the Three Rivers (not to scale), where "M" = mass flow, "Q" = flow rate, and "C" = OMP concentration. The dash box indicates the boundary for mass flow analysis.

Table 7. Percent contributions of OMP mass flows in the Three Rivers

	PHAR (%)	**HHIND (%)**	**PEST (%)**	**Flow (%)**
R1 (Seneca River)	30.5±9.1	37.8±11.3	56.2±24.5	40.5±13.2
R4 (Oneida River)	28.2±5.9	34.7±8.7	13.7±7.4	32.7±0.1
R5-R12 (Oswego River)	23.2±8.7	24.2±7.4	17.3±16.1	10.4±7.9
L4 (Onondaga Lake)	23.5±2.2	19.6±2.0	12.0±6.8	10.8±4.7
Sum	105.4±14.0	116.4±16.2	99.1±31.0	94.4±16.0

Chapter 4: Conclusions and Future Work

4.1 Conclusions

The Onondaga Lake-Three Rivers system is a regionally-important hydrologic feature in central New York. This thesis combines field sampling and high resolution mass spectrometry to characterize the occurrence patterns and mass flows of organic micropollutants (OMPs) in this lake-river system. Using a suspect screening workflow developed in this work, 52, 31, and 37 OMPs were identified and quantified in Onondaga Lake, its four major tributaries, and the Three Rivers, respectively. The optimized suspect screening workflow takes advantage of in-house suspect database matching and online mass spectral library search to prioritize and identify OMPs that had a high probability to occur in the lake and river water samples. In general, the concentrations of individual OMPs varied from low ng/L to low µg/L levels, consistent with those measured in other surface waters with wastewater inputs. Six OMPs, including lamotrigine, estradiol, benzotriazole, methyl benzotriazole, sucralose, and atrazine, occurred at relatively high concentrations with 100% detection frequency in all the samples, suggesting that this group of OMPs may serve as indicator compounds to guide future monitoring programs.

The horizontal concentration profiles of OMPs in Onondaga Lake were relatively consistent over the sampling period, but the vertical distribution of OMPs in the lake was strongly affected by thermal stratification and wastewater discharge. Peak concentrations of OMPs were observed within the thermocline in July 2017, likely due to the entry of negatively buoyant wastewater effluent. Principal component analysis further revealed that OMPs present in Onondaga Lake originated from either point wastewater discharge from the nearby WWTP or diffuse inputs from the lake watershed associated with agricultural activities or irregular

wastewater discharge (e.g., leaky sewers or combined sewer overflows), although no apparent correlation between OMP occurrence and land use in the tributary subwatersheds was identified. On the other hand, the longitudinal concentration profiles of OMPs in the Three Rivers suggested a continuous input of OMPs into the rivers. Mass flow calculations revealed that the WWTP served as the dominant source of OMPs present in Onondaga Lake, accounting for up to 67-86% of the OMP mass flow entering the lake. Onondaga Lake itself accounted for 12-24% of the OMP mass flow entering the Three Rivers, confirming its role as a regionally important source of OMPs.

4.2 Future Work

While the suspect screening workflow developed in this thesis prioritized and identified several dozens of OMPs in the Onondaga Lake-Three Rivers system, further method development is desirable to improve the mass spectral library search and *in silico* fragmentation for structural identification of suspect OMPs. For a methodological perspective, the mass spectral library search can be expanded to incorporate other mass spectral databases such as MassBank for a broader coverage and the *in silico* fragmentation can be supplemented with other computational tools such as MetFrag or CFM-ID to allow more efficient predictions of tandem mass spectra. Application of non-target screening to identify previously undetected or unanticipated OMPs is also an important direction to consider, although proper workflow optimization and data prioritization are needed.

Future work should also explore the utility of combining geospatial analysis and statistical tools to better pinpoint the sources of OMPs, particularly those originating from diffuse sources. Several recent studies have demonstrated how these tools can be integrated with suspect or non-

target screening to facilitate identification of OMP hotspots at the watershed scale. More importantly, such multi-faceted analysis may provide a knowledge base from which targeted management strategies can be implemented to control the sources of OMPs.

Lastly, additional laboratory and field-based studies should be conducted to assess the fate of OMPs in the lake-river system studied herein. Most OMPs are known to undergo abiotic or biotic transformations once released into the aquatic environment. Understanding possible depth-dependent transformation pathways such as photodegradation in the photic zone and biodegradation in the water column would serve as the basis for a more accurate assessment of the persistence and ecotoxicological risks of OMPs. Furthermore, coupling transformation data with hydrodynamic modeling would better constrain the spatiotemporal extent of OMP occurrence.

Appendix

Table A 1. List of 51 OMPs used for the development of suspect screening workflow

CAS No.	Compound Name	Molecular Formula	Exact Mass	RT (min)	Log*P*	Category
57-41-0	Phenytoin	C15 H12 N2 O2	252.0899	13.29	2.15	PHAR
136470-78-5	Abacavir	C14 H18 N6 O	286.3320	8.65	0.39	PHAR
135410-20-7	Acetamiprid	C10 H11 Cl N4	222.0672	10.93	1.11	PHAR
50-48-6	Amitriptyline	C20 H23 N	277.1831	15.40	4.81	PHAR
63-05-8	Androstenedione	C19 H26 O2	286.1933	17.38	3.93	PHAR
1912-24-9	Atrazine	C8 H14 Cl N5	215.0938	15.46	2.20	PEST
519-09-5	Benzoylecgonine	C16 H19 N O4	289.1314	9.77	-0.59	PHAR
34911-55-2	Bupropion	C13 H18 Cl N O	239.1077	11.83	3.27	PHAR
298-46-4	Carbamazepine	C15 H12 N2 O	236.0950	14.68	2.77	PHAR
10605-21-7	Carbendazim	C9 H9 N3 O2	191.0695	6.76	1.80	PEST
1563-66-2	Carbofuran	C12 H15 N O3	221.1052	13.90	2.05	PEST
59729-33-8	Citalopram	C20 H21 F N2 O	324.1638	13.11	3.76	PHAR
134-62-3	DEET	C12 H17 N O	191.1310	15.75	2.50	PEST
6190-65-4	Atrazine-desethyl	C6 H10 Cl N5	187.6300	11.44	1.54	PEST
125-71-3	Dextromethorphan	C18 H25 N O	271.1936	13.08	3.49	PHAR
439-14-5	Diazepam	C16 H13 Cl N2 O	284.7430	17.45	3.08	PHAR
84-66-2	Diethyl phthalate	C12 H14 O4	222.0892	16.07	2.69	HHIND
42399-41-7	Diltiazem	C22 H26 N2 O4 S	414.1613	13.88	2.73	PHAR
50563-36-5	Dimethachlor	C13 H18 Cl N O2	255.1026	16.28	2.59	PEST
131-11-3	Dimethyl phthalate	C10 H10 O4	194.0579	13.18	1.98	PEST
58-73-1	Diphenhydramine	C17 H21 N O	255.1623	13.22	3.65	PHAR
83799-24-0	Fexofenadine	C32 H39 N O4	501.2879	14.98	2.94	PHAR
54143-55-4	Flecainide	C17 H20 F6 N2 O3	414.1378	13.11	3.19	PHAR
86386-73-4	Fluconazole	C13 H12 F2 N6 O	306.1041	11.06	0.56	PHAR
2164-17-2	Fluometuron	C10 H11 F3 N2 O	232.0824	15.06	2.20	PHAR
60142-96-3	Gabapentin	C9 H17 N O2	171.1259	7.34	-1.27	PHAR
138402-11-6	Irbesartan	C25 H28 N6 O	428.2325	16.48	5.39	PHAR
34123-59-6	Isoproturon	C12 H18 N2 O	206.1419	15.82	2.57	PEST
6740-88-1	Ketamine	C13 H16 Cl N O	237.0920	9.80	3.35	PHAR
14769-73-4	Levamisole	C11 H12 N2 S	204.0721	5.83	2.36	PHAR
57837-19-1	Metalaxyl	C15 H21 N O4	279.1471	15.89	2.12	PEST
76-99-3	Methadone	C21 H27 N O	309.2093	15.20	5.01	PEST
532-03-6	Methocarbamol	C11 H15 N O5	241.0950	11.28	0.45	PHAR
51218-45-2	Metolachlor	C15 H22 Cl N O2	283.1339	19.10	3.45	PEST
51384-51-1	Metoprolol	C15 H25 N O3	267.1834	10.60	1.76	PHAR
21312-10-7	N4-Acetylsulfamethoxazole	C12 H13 N3 O4 S	295.0627	11.31	0.86	PHAR
42200-33-9	Nadolol	C17 H27 N O4	309.1940	9.06	0.87	PHAR

CAS No.	Compound Name	Molecular Formula	Exact Mass	RT (min)	Log*P*	Category
28721-07-5	Oxcarbazepine	C15 H12 N2 O2	252.0899	12.69	1.82	PHAR
60-80-0	Antipyrine	C11 H12 N2 O	188.0950	10.00	1.22	PHAR
1610-18-0	Prometon	C10 H19 N5 O	225.2900	13.38	2.23	PEST
139-40-2	Propazine	C9 H16 Cl N5	229.1094	17.12	2.61	PHAR
3506-09-0	Propranolol	C16 H21 N O2	259.1572	13.05	2.58	PHAR
79617-96-2	Sertraline	C17 H17 Cl2 N	305.0738	16.60	5.15	PEST
1982-49-6	Siduron	C14 H20 N2 O	232.1576	17.23	3.27	PEST
122-34-9	Simazine	C7 H12 Cl N5	201.0781	13.62	1.78	PEST
5915-41-3	Terbuthylazine	C9 H16 Cl N5	229.1094	17.47	2.48	PHAR
58-22-0	Testosterone	C19 H28 O2	288.2089	18.30	3.37	PHAR
111988-49-9	Thiacloprid	C10 H9 Cl N4 S	252.7200	11.78	2.06	PEST
738-70-5	Trimethoprim	C14 H18 N4 O3	290.1379	8.45	1.28	PHAR
115-96-8	Tris(2-chloroethyl) phosphate	C6 H12 Cl3 O4 P	283.9539	14.09	2.11	PEST
93413-69-5	Venlafaxine	C17 H27 N O2	277.2042	12.49	2.74	PHAR

References

(1) Schwarzenbach, R. P. The Challenge of Micropollutants in Aquatic Systems. *Science (80-.).* **2006**, *313* (5790), 1072–1077.

(2) Kolpin, D. W.; Furlong, E. T.; Meyer, M. T.; Thurman, E. M.; Zaugg, S. D.; Barber, L. B.; Buxton, H. T. Pharmaceuticals, Hormones, and Other Organic Wastewater Contaminants in U.S. Streams, 1999−2000: A National Reconnaissance. *Environ. Sci. Technol.* **2002**, *36* (6), 1202–1211.

(3) Escher, B. I.; Fenner, K. Recent Advances in Environmental Risk Assessment of Transformation Products. *Environ. Sci. Technol.* **2011**, *45*, 3835–3847.

(4) Reungoat, J.; Escher, B. I.; Macova, M.; Keller, J. Biofiltration of Wastewater Treatment Plant Effluent: Effective Removal of Pharmaceuticals and Personal Care Products and Reduction of Toxicity. *Water Res.* **2011**, *45* (9), 2751–2762.

(5) Hug, C.; Ulrich, N.; Schulze, T.; Brack, W.; Krauss, M. Identification of Novel Micropollutants in Wastewater by a Combination of Suspect and Nontarget Screening. *Environ. Pollut.* **2014**, *184*, 25–32.

(6) Farré, M. la; Pérez, S.; Kantiani, L.; Barceló, D. Fate and Toxicity of Emerging Pollutants, Their Metabolites and Transformation Products in the Aquatic Environment. *TrAC - Trends Anal. Chem.* **2008**, *27* (11), 991–1007.

(7) Owens, E. M.; Effler, S. W.; Matthews, D. A.; Prestigiacomo, A. R. Evaluation of Offshore Wastewater Outfall and Diffuser for Onondaga Lake , NY. **2013**, *2013* (September), 1–15.

(8) Baumgartner, R. Transformations of Novel and Unconventional Organic Compounds in Engineered and Natural Systems : Fluoroaromatics and Biodegradable Polyesters. **2014**,

No. 22364.

(9) Carpenter, C. M. G.; Helbling, D. E. Removal of Micropollutants in Biofilters: Hydrodynamic Effects on Biofilm Assembly and Functioning. *Water Res.* **2017**, *120*, 211–221.

(10) Conley, J. M.; Evans, N.; Mash, H.; Rosenblum, L.; Schenck, K.; Glassmeyer, S.; Furlong, E. T.; Kolpin, D. W.; Wilson, V. S. Comparison of in Vitro Estrogenic Activity and Estrogen Concentrations in Source and Treated Waters from 25 U.S. Drinking Water Treatment Plants. *Sci. Total Environ.* **2017**, *579*, 1610–1617.

(11) Karpuzcu, M. E.; Fairbairn, D.; Arnold, W. A.; Barber, B. L.; Kaufenberg, E.; Koskinen, W. C.; Novak, P. J.; Rice, P. J.; Swackhamer, D. L. Identifying Sources of Emerging Organic Contaminants in a Mixed Use Watershed Using Principal Components Analysis. *Environ. Sci. Process. Impacts* **2014**, *16* (10), 2390–2399.

(12) Phillips, P.; Chalmers, A. Wastewater Effluent, Combined Sewer Overflows, and Other Sources of Organic Compounds to Lake Champlain. *J. Am. Water Resour. Assoc.* **2009**, *45* (1), 45–57.

(13) Bradley, P. M.; Journey, C. A.; Romanok, K. M.; Barber, L. B.; Buxton, H. T.; Foreman, W. T.; Furlong, E. T.; Glassmeyer, S. T.; Hladik, M. L.; Iwanowicz, L. R.; et al. Expanded Target-Chemical Analysis Reveals Extensive Mixed-Organic-Contaminant Exposure in U.S. Streams. *Environ. Sci. Technol.* **2017**, *51* (9), 4792–4802.

(14) Cantwell, M. G.; Katz, D. R.; Sullivan, J. C.; Shapley, D.; Lipscomb, J.; Epstein, J.; Juhl, A. R.; Knudson, C.; Mullan, G. D. O. Spatial Patterns of Pharmaceuticals and Wastewater Tracers in the Hudson River Estuary. *Water Res.* **2018**, *137*, 335–343.

(15) Carpenter, C.; Helbling, D. E. Widespread Micropollutant Monitoring in the Hudson

River Estuary Reveals Spatiotemporal Micropollutant Clusters and Their Sources. *Environ. Sci. Technol.* **2018**, *52*, 6187–6196.

(16) Phillips, P. J.; Bode, R. W. Pesticides in Surface Water Runoff in South-Eastern New York State, USA: Seasonal and Stormflow Effects on Concentrations. *Pest Manag. Sci.* **2004**, *60* (6), 531–543.

(17) Phillips, P. J.; Gibson, C. A.; Fisher, S. C.; Fisher, I. J.; Reilly, T. J.; Smalling, K. L.; Romanok, K. M.; Foreman, W. T.; ReVello, R. C.; Focazio, M. J.; et al. Regional Variability in Bed-Sediment Concentrations of Wastewater Compounds, Hormones and PAHs for Portions of Coastal New York and New Jersey Impacted by Hurricane Sandy. *Mar. Pollut. Bull.* **2016**, *107* (2), 489–498.

(18) Benotti, B. M. J.; Fisher, S. C.; Terracciano, S. A.; Survey, U. S. G. Occurrence of Pharmaceuticals in Shallow Ground Water of Suffolk County , New York , 2002 – 2005. **2006**, 2002–2005.

(19) Hughes, S. R.; Kay, P.; Brown, L. E. Global Synthesis and Critical Evaluation of Pharmaceutical Data Sets Collected from River Systems. *Environ. Sci. Technol.* **2013**, *47* (2), 661–677.

(20) Bernhardt, E. S.; Rosi, E. J.; Gessner, M. O. Synthetic Chemicals as Agents of Global Change. *Front. Ecol. Environ.* **2017**, *15* (2), 84–90.

(21) Benotti, M. J.; Trenholm, R. A.; Vanderford, B. J.; Holady, J. C.; Stanford, B. D.; Snyder, S. A. Pharmaceuticals and Endocrine Disrupting Compounds in U.S. Drinking Water. *Environ. Sci. Technol.* **2009**, *43* (3), 597–603.

(22) Richardson, S. D.; Ternes, T. A. Water Analysis: Emerging Contaminants and Current Issues. *Anal. Chem.* **2014**, *86* (6), 2813–2848.

(23) Reemtsma, T.; Berger, U.; Arp, H. P. H.; Gallard, H.; Knepper, T. P.; Neumann, M.; Quintana, J. B.; Voogt, P. De. Mind the Gap: Persistent and Mobile Organic Compounds - Water Contaminants That Slip Through. *Environ. Sci. Technol.* **2016**, *50* (19), 10308–10315.

(24) aus der Beek, T.; Weber, F. A.; Bergmann, A.; Hickmann, S.; Ebert, I.; Hein, A.; Küster, A. Pharmaceuticals in the Environment-Global Occurrences and Perspectives. *Environ. Toxicol. Chem.* **2016**, *35* (4), 823–835.

(25) Batt, A. L.; Kincaid, T. M.; Kostich, M. S.; Lazorchak, J. M.; Olsen, A. R. Evaluating the Extent of Pharmaceuticals in Surface Waters of the United States Using a National-Scale Rivers and Streams Assessment Survey. *Environ. Toxicol. Chem.* **2016**, *35* (4), 874–881.

(26) Barnes, K. K.; Kolpin, D. W.; Furlong, E. T.; Zaugg, S. D.; Meyer, M. T.; Barber, L. B. A National Reconnaissance of Pharmaceuticals and Other Organic Wastewater Contaminants in the United States--I) Groundwater. *Sci. Total Environ.* **2008**, *402* (2–3), 192–200.

(27) Furlong, E. T.; Batt, A. L.; Glassmeyer, S. T.; Noriega, M. C.; Kolpin, D. W.; Mash, H.; Schenck, K. M. Nationwide Reconnaissance of Contaminants of Emerging Concern in Source and Treated Drinking Waters of the United States: Pharmaceuticals. *Sci. Total Environ.* **2017**, *579*, 1629–1642.

(28) Subedi, B.; Codru, N.; Dziewulski, D. M.; Wilson, L. R.; Xue, J.; Yun, S.; Braun-Howland, E.; Minihane, C.; Kannan, K. A Pilot Study on the Assessment of Trace Organic Contaminants Including Pharmaceuticals and Personal Care Products from On-Site Wastewater Treatment Systems along Skaneateles Lake in New York State, USA. *Water Res.* **2014**, *72*, 28–39.

(29) Phillips, P. J.; Schubert, C.; Argue, D.; Fisher, I.; Furlong, E. T.; Foreman, W.; Gray, J.; Chalmers, A. Concentrations of Hormones, Pharmaceuticals and Other Micropollutants in Groundwater Affected by Septic Systems in New England and New York. *Sci. Total Environ.* **2015**, *512–513*, 43–54.

(30) Tilman, D.; Fargione, J.; Wolff, B.; Antonio, C. D.; Dobson, A.; Howarth, R.; Schindler, D.; Schlesinger, W. H.; Simberloff, D.; Swackhamer, D. Forecasting Agriculturally Driven Environmental Change. *Am. Assoc. fo rthe Adv. file///C/Users/Livia/OneDrive/DOCUMENTOS/Doutorado/artigos/Cabellos 2015.pdfof Sci.* **2001**, *292* (5515), 281–284.

(31) Beketov, M. A.; Kefford, B. J.; Schafer, R. B.; Liess, M. Pesticides Reduce Regional Biodiversity of Stream Invertebrates. *Proc. Natl. Acad. Sci.* **2013**, *110* (27), 11039–11043.

(32) Stehle, S.; Schulz, R. Agricultural Insecticides Threaten Surface Waters at the Global Scale. *Proc. Natl. Acad. Sci.* **2015**, *112* (18), 5750–5755.

(33) Gilliom, R. J. Pesticides in U.S. Streams and Groundwater. *Environ. Sci. Technol.* **2007**, *41* (10), 3408–3414.

(34) Stone, W. W.; Gilliom, R. J.; Ryberg, K. R. Pesticides in U.S. Streams and Rivers: Occurrence and Trends during 1992-2011. *Environ. Sci. Technol.* **2014**, *48* (19), 11025–11030.

(35) Brausch, J. M.; Rand, G. M. A Review of Personal Care Products in the Aquatic Environment: Environmental Concentrations and Toxicity. *Chemosphere* **2011**, *82* (11), 1518–1532.

(36) Ternes, T. A.; Joss, A.; Siegrist, H. Peer Reviewed: Scrutinizing Pharmaceuticals and Personal Care Products in Wastewater Treatment. *Environ. Sci. Technol.* **2004**, *38* (20),

392A–399A.

(37) Daughton, C. G.; Ternes, T. A. Pharmaceuticals and Personal Care Products in the Environment: Agents of Subtle Change? *Environ. Health Perspect.* **1999**, *107 Suppl* (12), 907–938.

(38) Kolpin, D. W.; Furlong, E. T.; Meyer, M. T.; Thurman, E. M.; Zaugg, S. D.; Barber, L. B.; Buxton, H. T. Pharmaceuticals, Hormones, and Other Organic Wastewater Contaminants in U.S. Streams, 1999-2000: A National Reconnaissance. *Environ. Sci. Technol.* **2002**, *36* (6), 1202–1211.

(39) Halden, R. U.; Paull, D. H. Co-Occurrence of Triclocarban and Triclosan in U.S. Water Resources. *Environ. Sci. Technol.* **2005**, *39* (6), 1420–1426.

(40) Fairbairn, D. J.; Arnold, W. A.; Barber, B. L.; Kaufenberg, E. F.; Koskinen, W. C.; Novak, P. J.; Rice, P. J.; Swackhamer, D. L. Contaminants of Emerging Concern: Mass Balance and Comparison of Wastewater Effluent and Upstream Sources in a Mixed-Use Watershed. *Environ. Sci. Technol.* **2016**, *50* (1), 36–45.

(41) Musolff, A.; Leschik, S.; Reinstorf, F.; Strauch, G.; Schirmer, M. Micropollutant Loads in the Urban Water Cycle. *Environ. Sci. Technol.* **2010**, *44* (13), 4877–4883.

(42) Eggen, R. I. L.; Hollender, J.; Joss, A.; Schärer, M.; Stamm, C. Reducing the Discharge of Micropollutants in the Aquatic Environment: The Benefits of Upgrading Wastewater Treatment Plants. *Environ. Sci. Technol.* **2014**, *48* (14), 7683–7689.

(43) Boxall, A. B. A.; Sinclair, C. J.; Fenner, K.; Kolpin, D.; Maund, S. J. Peer Reviewed: When Synthetic Chemicals Degrade in the Environment. *Environ. Sci. Technol.* **2004**, *38* (19), 368A–375A.

(44) Cwiertny, D. M.; Snyder, S. A.; Schlenk, D.; Kolodziej, E. P. Environmental Designer

Drugs: When Transformation May Not Eliminate Risk. *Environ. Sci. Technol.* **2014**, *48* (20), 11737–11745.

(45) Latch, D. E.; Packer, J. L.; Stender, B. L.; VanOverbeke, J.; Arnold, W. A.; McNeill, K. AQUEOUS PHOTOCHEMISTRY OF TRICLOSAN: FORMATION OF 2,4-DICHLOROPHENOL, 2,8-DICHLORODIBENZO-p-DIOXIN, AND OLIGOMERIZATION PRODUCTS. *Environ. Toxicol. Chem.* **2005**, *24* (3), 517.

(46) Qu, S.; Kolodziej, E. P.; Long, S. A.; Gloer, J. B.; Patterson, E. V.; Baltrusaitis, J.; Jones, G. D.; Benchetler, P. V.; Cole, E. A.; Kimbrough, K. C.; et al. Product-to-Parent Reversion of Trenbolone: Unrecognized Risks for Endocrine Disruption. *Science (80-.).* **2013**, *342* (6156), 347–351.

(47) García-Galán, M. J.; Anfruns, A.; Gonzalez-Olmos, R.; Rodríguez-Mozaz, S.; Comas, J. UV/H2O2degradation of the Antidepressants Venlafaxine and O-Desmethylvenlafaxine: Elucidation of Their Transformation Pathway and Environmental Fate. *J. Hazard. Mater.* **2016**, *311*, 70–80.

(48) von Gunten, U. Ozonation of Drinking Water: Part II. Disinfection and by-Product Formation in Presence of Bromide, Iodide or Chlorine. *Water Res.* **2003**, *37* (7), 1469–1487.

(49) Sumpter, J. P.; Johnson, A. C. Lessons from Endocrine Disruption and Their Application to Other Issues Concerning Trace Organics in the Aquatic Environment. *Environmental Science and Technology*. 2005, pp 4321–4332.

(50) Mills, L. J.; Chichester, C. Review of Evidence: Are Endocrine-Disrupting Chemicals in the Aquatic Environment Impacting Fish Populations? *Science of the Total Environment*. 2005, pp 1–34.

(51) Tyler, C. R.; Jobling, S. Roach, Sex, and Gender-Bending Chemicals: The Feminization of Wild Fish in English Rivers. *Bioscience* **2008**, *58* (11), 1051.

(52) Jobling, S.; Nolan, M.; Tyler, C. R.; Brighty, G.; Sumpter, J. P. Widespread Sexual Disruption in Wild Fish. *Environ. Sci. Technol.* **1998**, *32* (17), 2498–2506.

(53) Alan, M. V.; Barber, L. B.; Gray, J. L.; Lopez, E. M.; Woodling, J. D.; Norris, D. O. Reproductive Disruption in Fish Downstream from an Estrogenic Wastewater Effluent. *Environ. Sci. Technol.* **2008**, *42* (9), 3407–3414.

(54) Hayes, T. B.; Khoury, V.; Narayan, A.; Nazir, M.; Park, A.; Brown, T.; Adame, L.; Chan, E.; Buchholz, D.; Stueve, T.; et al. Atrazine Induces Complete Feminization and Chemical Castration in Male African Clawed Frogs (Xenopus Laevis). *Proc. Natl. Acad. Sci.* **2010**, *107* (10), 4612–4617.

(55) Kidd, K. A.; Blanchfield, P. J.; Mills, K. H.; Palace, V. P.; Evans, R. E.; Lazorchak, J. M.; Flick, R. W. Collapse of a Fish Population after Exposure to a Synthetic Estrogen. *Proc. Natl. Acad. Sci.* **2007**, *104* (21), 8897–8901.

(56) Haack, S. K.; Metge, D. W.; Fogarty, L. R.; Meyer, M. T.; Barber, L. B.; Harvey, R. W.; Leblanc, D. R.; Kolpin, D. W. Effects on Groundwater Microbial Communities of an Engineered 30-Day in Situ Exposure to the Antibiotic Sulfamethoxazole. *Environ. Sci. Technol.* **2012**, *46* (14), 7478–7486.

(57) Rosi, E. J.; Bechtold, H. A.; Snow, D.; Rojas, M.; Reisinger, A. J.; Kelly, J. J. Urban Stream Microbial Communities Show Resistance to Pharmaceutical Exposure. *Ecosphere* **2018**, *9* (1), e02041.

(58) Schollée, J. E.; Schymanski, E. L.; Avak, S. E.; Loos, M.; Hollender, J. Prioritizing Unknown Transformation Products from Biologically-Treated Wastewater Using High-

Resolution Mass Spectrometry, Multivariate Statistics, and Metabolic Logic. *Anal. Chem.* **2015**, *87* (24), 12121–12129.

(59) Ruff, M.; Mueller, M. S.; Loos, M.; Singer, H. P. Quantitative Target and Systematic Non-Target Analysis of Polar Organic Micro-Pollutants along the River Rhine Using High-Resolution Mass- Spectrometry e Identi Fi Cation of Unknown Sources and Compounds. *Water Res.* **2015**, *87*, 145–154.

(60) Moschet, C.; Wittmer, I.; Simovic, J.; Junghans, M.; Piazzoli, A.; Singer, H.; Stamm, C.; Leu, C.; Hollender, J. How a Complete Pesticide Screening Changes the Assessment of Surface Water Quality. *Environ. Sci. Technol.* **2014**, *48* (10), 5423–5432.

(61) Park, N.; Choi, Y.; Kim, D.; Kim, K.; Jeon, J. Prioritization of Highly Exposable Pharmaceuticals via a Suspect/Non-Target Screening Approach: A Case Study for Yeongsan River, Korea. *Sci. Total Environ.* **2018**, *639*, 570–579.

(62) Krauss, M.; Singer, H.; Hollender, J. LC-High Resolution MS in Environmental Analysis: From Target Screening to the Identification of Unknowns. *Anal. Bioanal. Chem.* **2010**, *397* (3), 943–951.

(63) Pochodylo, A. L.; Helbling, D. E. Emerging Investigators Series: Prioritization of Suspect Hits in a Sensitive Suspect Screening Workflow for Comprehensive Micropollutant Characterization in Environmental Samples. *Environ. Sci. Water Res. Technol.* **2017**, *3* (1), 54–65.

(64) Bletsou, A. A.; Jeon, J.; Hollender, J.; Archontaki, E.; Thomaidis, N. S. Targeted and Non-Targeted Liquid Chromatography-Mass Spectrometric Workflows for Identification of Transformation Products of Emerging Pollutants in the Aquatic Environment. *TrAC - Trends Anal. Chem.* **2015**, *66*, 32–44.

(65) Schymanski, E. L.; Singer, H. P.; Slobodnik, J.; Ipolyi, I. M.; Oswald, P.; Krauss, M.; Schulze, T.; Haglund, P.; Letzel, T.; Grosse, S.; et al. Non-Target Screening with High-Resolution Mass Spectrometry: Critical Review Using a Collaborative Trial on Water Analysis. *Anal. Bioanal. Chem.* **2015**, *407* (21), 6237–6255.

(66) Gago-Ferrero, P.; Schymanski, E. L.; Bletsou, A. A.; Aalizadeh, R.; Hollender, J.; Thomaidis, N. S. Extended Suspect and Non-Target Strategies to Characterize Emerging Polar Organic Contaminants in Raw Wastewater with LC-HRMS/MS. *Environ. Sci. Technol.* **2015**, *49* (20), 12333–12341.

(67) Moschet, C.; Piazzoli, A.; Singer, H.; Hollender, J. Alleviating the Reference Standard Dilemma Using a Systematic Exact Mass Suspect Screening Approach with Liquid Chromatography-High Resolution Mass Spectrometry. *Anal. Chem.* **2013**, *85* (21), 10312–10320.

(68) Zedda, M.; Zwiener, C. Is Nontarget Screening of Emerging Contaminants by LC-HRMS Successful? A Plea for Compound Libraries and Computer Tools. *Analytical and Bioanalytical Chemistry*. 2012, pp 2493–2502.

(69) Chiaia-Hernández, A. C.; Günthardt, B. F.; Frey, M. P.; Hollender, J. Unravelling Contaminants in the Anthropocene Using Statistical Analysis of Liquid Chromatography–High-Resolution Mass Spectrometry Nontarget Screening Data Recorded in Lake Sediments. *Environ. Sci. Technol.* **2017**, *51* (21), 12547–12556.

(70) Richardson, S. D.; Kimura, S. Y. Water Analysis: Emerging Contaminants and Current Issues. *Analytical Chemistry*. 2016, pp 546–582.

(71) Ruttkies, C.; Schymanski, E. L.; Wolf, S.; Hollender, J.; Neumann, S. MetFrag Relaunched: Incorporating Strategies beyond in Silico Fragmentation. *J. Cheminform.*

2016, *8* (1), 1–16.

(72) Hollender, J.; Schymanski, E. L.; Singer, H.; Ferguson, P. L. Non-Target Screening with High Resolution Mass Spectrometry in the Environment: Ready to Go? *Environ. Sci. Technol.* **2017**, No. 1, acs.est.7b02184.

(73) Gago-Ferrero, P.; Krettek, A.; Fischer, S.; Wiberg, K.; Ahrens, L. Suspect Screening and Regulatory Databases: A Powerful Combination to Identify Emerging Micropollutants. *Environ. Sci. Technol.* **2018**.

(74) Effler, S. W. *Limnological and Engineering Analysis of Polluted Urban Lake*; Effler, S. W., Ed.; Springer Series on Environmental Management; Springer New York: New York, NY, 1996.

(75) Effler, S. W.; Hennigan, R. D. Onondaga Lake, New York: Legacy of Pollution. *Lake and Reservoir Management*. 1996, pp 1–12.

(76) Effler, S. W.; Drlscoll, C. T. Calcium Chemistry and Deposition in Ionically Enriched Onondaga Lake, New York†. *Environ. Sci. Technol.* **1985**, *19* (8), 716–720.

(77) Effler, S. W.; Prestigiacomo, A. R.; Effler, A. J. P.; Driscoll, C. Water Quality Patterns in a River-Lake System from Multiple Drivers (Three Rivers, New York State). *River Syst.* **2010**, *19* (1), 75–94.

(78) Effler, S. W.; O'Donnell, D. M.; Owen, C. J. America's Most Polluted Lake: Using Robotic Buoys to Monitor the Rehabilitation of Onondaga Lake. *J. Urban Technol.* **2002**, *9* (2), 21–44.

(79) Matthews, D. A.; Effler, S. W. Assessment of Long-Term Trends in the Oxygen Resources of a Recovering Urban Lake, Onondaga Lake, New York. *Lake Reserv. Manag.* **2006**, *22* (1), 19–32.

(80) Effler, S. W.; Hennigan, R. D. Onondaga Lake, New York: Legacy of Pollution. *Lake Reserv. Manag.* **1996**, *12* (1), 1–12.

(81) Kern, S.; Fenner, K.; Singer, H. P.; Schwarzenbach, R. P.; Hollender, J. Identification of Transformation Products of Organic Contaminants in Natural Waters by Computer-Aided Prediction and High-Resolution Mass Spectrometry. *Environ. Sci. Technol.* **2009**, *43* (18), 7039–7046.

(82) Schymanski, E. L.; Meringer, M.; Brack, W. Matching Structures to Mass Spectra Using Fragmentation Patterns: Are the Results As Good As They Look? *Anal. Chem.* **2009**, *81* (9), 3608–3617.

(83) De Vijlder, T.; Valkenborg, D.; Lemière, F.; Romijn, E. P.; Laukens, K.; Cuyckens, F. A Tutorial in Small Molecule Identification via Electrospray Ionization-Mass Spectrometry: The Practical Art of Structural Elucidation. *Mass Spectrom. Rev.* **2017**, No. October 2017, 1–23.

(84) Schymanski, E. L.; Singer, H. P.; Longrée, P.; Loos, M.; Ruff, M.; Stravs, M. A.; Ripollés Vidal, C.; Hollender, J. Strategies to Characterize Polar Organic Contamination in Wastewater: Exploring the Capability of High Resolution Mass Spectrometry. *Environ. Sci. Technol.* **2014**, *48* (3), 1811–1818.

(85) Bonvin, F.; Rutler, R.; Chavre, N.; Halder, J.; Kohn, T. Spatial and Temporal Presence of a Wastewater-Derived Micropollutant Plume in Lake Geneva. *Environ. Sci. Technol.* **2011**, *45* (11), 4702–4709.

(86) Moschet, C.; Götz, C.; Longrée, P.; Hollender, J.; Singer, H. Multi-Level Approach for the Integrated Assessment of Polar Organic Micropollutants in an International Lake Catchment: The Example of Lake Constance. *Environ. Sci. Technol.* **2013**, *47* (13), 7028–

7036.

(87) Richardson, S. D.; Ternes, T. A. Water Analysis: Emerging Contaminants and Current Issues. *Anal. Chem.* **2018**, *90* (1), 398–428.

(88) Soh, L.; Connors, K. A.; Brooks, B. W.; Zimmerman, J. Fate of Sucralose through Environmental and Water Treatment Processes and Impact on Plant Indicator Species. *Environ. Sci. Technol.* **2011**, *45* (4), 1363–1369.

(89) Torres, C. I.; Ramakrishna, S.; Chiu, C.; Nelson, K. G.; Westerhoff, P.; Krajmalnik-Brown, R. Fate of Sucralose During Wastewater Treatment. *Environ. Eng. Sci.* **2011**, *28* (5), 325–331.

(90) Loos, R.; Gawlik, B. M.; Boettcher, K.; Locoro, G.; Contini, S.; Bidoglio, G. Sucralose Screening in European Surface Waters Using a Solid-Phase Extraction-Liquid Chromatography-Triple Quadrupole Mass Spectrometry Method. *J. Chromatogr. A* **2009**, *1216* (7), 1126–1131.

(91) Scheurer, M.; Brauch, H. J.; Lange, F. T. Analysis and Occurrence of Seven Artificial Sweeteners in German Waste Water and Surface Water and in Soil Aquifer Treatment (SAT). *Anal. Bioanal. Chem.* **2009**, *394* (6), 1585–1594.

(92) Moschet, C.; Lew, B. M.; Hasenbein, S.; Anumol, T.; Young, T. M. LC- and GC-QTOF-MS as Complementary Tools for a Comprehensive Micropollutant Analysis in Aquatic Systems. *Environ. Sci. Technol.* **2017**, *51* (3), 1553–1561.

(93) Mead, R. N.; Morgan, J. B.; Avery, G. B.; Kieber, R. J.; Kirk, A. M.; Skrabal, S. A.; Willey, J. D. Occurrence of the Artificial Sweetener Sucralose in Coastal and Marine Waters of the United States. *Mar. Chem.* **2009**, *116* (1–4), 13–17.

(94) Ferrer, I.; Thurman, E. M. Analysis of Sucralose and Other Sweeteners in Water and

Beverage Samples by Liquid Chromatography/Time-of-Flight Mass Spectrometry. *J. Chromatogr. A* **2010**, *1217* (25), 4127–4134.

(95) Oppenheimer, J.; Eaton, A.; Badruzzaman, M.; Haghani, A. W.; Jacangelo, J. G. Occurrence and Suitability of Sucralose as an Indicator Compound of Wastewater Loading to Surface Waters in Urbanized Regions. *Water Res.* **2011**, *45* (13), 4019–4027.

(96) Bernot, M. J.; Becker, J. C.; Doll, J.; Lauer, T. E. A National Reconnaissance of Trace Organic Compounds (TOCs) in United States Lotic Ecosystems. *Sci. Total Environ.* **2016**, *572*, 422–433.

(97) van Leerdam, J. A.; Hogenboom, A. C.; van der Kooi, M. M. E.; de Voogt, P. Determination of Polar 1H-Benzotriazoles and Benzothiazoles in Water by Solid-Phase Extraction and Liquid Chromatography LTQ FT Orbitrap Mass Spectrometry. *Int. J. Mass Spectrom.* **2009**, *282* (3), 99–107.

(98) Xu, W.; Yan, W.; Licha, T. Simultaneous Determination of Trace Benzotriazoles and Benzothiazoles in Water by Large-Volume Injection/Gas Chromatography-Mass Spectrometry. *J. Chromatogr. A* **2015**, *1422*, 270–276.

(99) Loos, R.; Locoro, G.; Comero, S.; Contini, S.; Schwesig, D.; Werres, F.; Balsaa, P.; Gans, O.; Weiss, S.; Blaha, L.; et al. Pan-European Survey on the Occurrence of Selected Polar Organic Persistent Pollutants in Ground Water. *Water Res.* **2010**, *44* (14), 4115–4126.

(100) Cancilla, D. A. Detection of Aircraft Deicing/Antiicing Fluid Additives in a Perched Water Monitoring Well at an International Airport. *Environ. Sci. Technol.* **1998**, *32* (23), 3834–3835.

(101) Giger, W.; Schaffner, C.; Kohler, H. P. E. Benzotriazole and Tolyltriazole as Aquatic Contaminants. 1. Input and Occurrence in Rivers and Lakes. *Environ. Sci. Technol.* **2006**,

40 (23), 7186–7192.

(102) Fries, E.; Gocht, T.; Klasmeier, J. Occurrence and Distribution of Benzothiazole in the Schwarzbach Watershed (Germany). *J. Environ. Monit.* **2011**, *13* (10), 2838–2843.

(103) Scheurer, M.; Michel, A.; Brauch, H. J.; Ruck, W.; Sacher, F. Occurrence and Fate of the Antidiabetic Drug Metformin and Its Metabolite Guanylurea in the Environment and during Drinking Water Treatment. *Water Res.* **2012**, *46* (15), 4790–4802.

(104) Scheurer, M.; Sacher, F.; Brauch, H. J. Occurrence of the Antidiabetic Drug Metformin in Sewage and Surface Waters in Germany. *J. Environ. Monit.* **2009**, *11* (9), 1608–1613.

(105) Vulliet, E.; Cren-Olivé, C. Screening of Pharmaceuticals and Hormones at the Regional Scale, in Surface and Groundwaters Intended to Human Consumption. *Environ. Pollut.* **2011**, *159* (10), 2929–2934.

(106) Khanal, S. K.; Xie, B.; Thompson, M. L.; Sung, S.; Ong, S. K.; Van Leeuwen, J. Fate, Transport and Biodegradation of Natural Estrogens in the Environment and Engineered Systems. *Environmental Science and Technology*. 2006, pp 6537–6546.

(107) Kolodziej, E. P.; Harter, T.; Sedlak, D. L. Dairy Wastewater, Aquaculture, and Spawning Fish as Sources of Steroid Hormones in the Aquatic Environment. *Environ. Sci. Technol.* **2004**, *38* (23), 6377–6384.

(108) Finlay-Moore, O.; Hartel, P. G.; Cabrera, M. L. 17β-Estradiol and Testosterone in Soil and Runoff from Grasslands Amended with Broiler Litter. *J. Environ. Qual.* **2000**, *29* (5), 1604.

(109) Matthiessen, P.; Arnold, D.; Johnson, A. C.; Pepper, T. J.; Pottinger, T. G.; Pulman, K. G. T. Contamination of Headwater Streams in the United Kingdom by Oestrogenic Hormones from Livestock Farms. *Sci. Total Environ.* **2006**, *367* (2–3), 616–630.

(110) Kolodziej, E. P.; Sedlak, D. L. Rangeland Grazing as a Source of Steroid Hormones to Surface Waters. *Environ. Sci. Technol.* **2007**, *41* (10), 3514–3520.

(111) Ferrer, I.; Thurman, E. M. Identification of a New Antidepressant and Its Glucuronide Metabolite in Water Samples Using Liquid Chromatography/Quadrupole Time-of-Flight Mass Spectrometry. (Special Issue: Environmental Analysis as Related to Climate Change.). *Anal. Chem.* **2010**, *82* (19), 8161–8168.

(112) Matthews, D. A.; Donnell, S. M. O.; Effler, S. W.; Owens, E. M.; Hurteau, C. A.; Prestigiacomo, A. R. Density , Salinity , and Entry Depths of Municipal Wastewater in an Urban Lake. **2012**.

(113) Schimmelpfennig, S.; Kirillin, G.; Engelhardt, C.; Dünnbier, U.; Nützmann, G. Fate of Pharmaceutical Micro-Pollutants in Lake Tegel (Berlin, Germany): The Impact of Lake-Specific Mechanisms. *Environ. Earth Sci.* **2016**, *75* (10).

(114) Canale, R. P.; Auer, M. T.; Owens, E. M.; Heidtke, T. M.; Effler, S. W. Modeling Fecal Coliform Bacteria-II. Model Development and Application. *Water Res.* **1993**, *27* (4), 703–714.

(115) Effler, S. W.; Prestigiacomo, A. R.; Matthews, D. A.; Michalenko, E. M.; Hughes, D. J. Partitioning Phosphorus Concentrations and Loads in Tributaries of a Recovering Urban Lake. *Lake Reserv. Manag.* **2009**, *25* (3), 225–239.

(116) Rhea, J. R.; Russell, K. T.; Moran, E.; Glaser, D.; Ku, W.; Mastriano, J. J. Impacts of Advanced Tertiary Treatment on the Nitrogen Cycling of a Hypereutrophic Lake: A Case for 303(D) Delisting. *Proc. Water Environ. Fed.* **2006**, *2006* (8), 4025–4037.

(117) Effler, S. W.; Matthews, D. A.; Brooks-Matthews, C. M.; Perkins, M. G.; Siegfried, C. A.; Hassett, J. M. WATER QUALITY IMPACTS AND INDICATORS OF METABOLIC

ACTIVITY OF THE ZEBRA MUSSEL INVASION OF THE SENECA RIVER. *J. Am. Water Resour. Assoc.* **2004**, *40* (3), 737–754.

(118) Effler, S. W.; Carter, C. F. SPATIAL VARIABILITY IN SELECTED PHYSICAL CHARACTERISTICS AND PROCESSES IN CROSS LAKE, NEW YORK. *J. Am. Water Resour. Assoc.* **1987**, *23* (2), 243–249.

Vita

Name of Author: Shiru Wang
Place of Birth: Wenzhou, China
Date of Birth: August 22, 1993
Undergraduate Education: Ningbo University, China
Graduate Education: Syracuse University, Syracuse, NY

Degrees Awarded
Bachelor of Science in Chemistry, Ningbo University, China, 2015

Honors and Awards
- Certificate of Merit, Division of Environmental Chemistry, American Chemical Society, 2018
- Engineering & Computer Science Research Day Poster Prize, Syracuse University, 2018
- GLRC Student Travel Award | Great Lakes Research Consortium, 2018
- Nelson L. Nemerow Memorial Scholarship, Syracuse University, 2017
- Outstanding Graduate, Ningbo University, 2014
- National Scholarship, The Ministry of Education of the People's Republic of China, 2013
- The New-Shoot Talent Program of Zhejiang Province, The Ministry of Education of Zhejiang Province, 2012
- First-Class Scholarship, Ningbo University, 2012

Professional Experience
- Graduate Teaching Assistant, Dept. of Civil and Environmental Engineering, Syracuse University, 2017-2018
- Undergraduate Research Mentor, Dept. of Civil and Environmental Engineering, Syracuse University, Spring 2018
- Research Assistant, Ningbo University, Ningbo, China, 2011-2014

Conference Presentations
- Shiru, W.; Perkins, M.; Matthews, D.; Zeng, T., Combining Suspect Screening and Fluorescence Analysis to Characterize Organic Micropollutants in Onondaga Lake, NY. The 255th American Chemical Society National Meeting, New Orleans, LA, 2018. (Platform presentation)
- Shiru, W.; Zeng, T., Non-Target Screening and Prioritization of Sulfamethoxazole Photolysis Products. The 255th American Chemical Society National Meeting, New Orleans, LA, 2018. (Platform presentation)
- Shiru, W.; Zeng, T., Identification of Phototransformation Products of Chemicals of Emerging Concern (CECs) by Suspect and Non-Target Screening. The 4th Annual New England Graduate Student Water Symposium (NEGSWS), Amherst, MA, 2017. (Platform presentation)
- Shiru, W.; Perkins, M.; Matthews, D.; Zeng, T., Combining HRMS-Based Suspect Screening and Statistical Analysis to Assess Chemicals of Emerging Concern in Onondaga Lake. Society of Environmental Toxicology and Chemistry (SETAC) North America 38th Annual Meeting, Minneapolis, Minnesota, 2017. (Platform presentation)