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ARTICLE

Freshwater Ecology

Environmental conditions explain variability in concentrations of nutrients but not emerging contaminants

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Abstract

Aquatic ecosystems are subjected to many chemical stressors, including nutrients and emerging contaminants like pharmaceuticals. While pharmaceutical concentrations in streams and rivers are often below the thresholds for acute toxicity, they nonetheless disrupt ecology through changes to organisms' physiology, metabolism, and behavior. However, analyzing samples for the wide range of manufactured pharmaceuticals is often prohibitively expensive for many monitoring efforts. As such, the ability to predict pharmaceutical concentrations over space and time using easier-to-monitor water quality parameters would expand our understanding of the scope and consequences of pharmaceutical contamination in aquatic ecosystems. We applied random forest models to data from the Baltimore Ecosystem Study to investigate how well routinely monitored water quality parameters could be used to predict concentrations of nutrients and pharmaceuticals. We found that concentrations of nutrients were accurately predicted by these models, but models for predicting concentrations of pharmaceuticals had high error rates and low predictive ability. Differences in our ability to predict concentrations of nutrients as opposed to pharmaceuticals could be due to differences in their sources, chemistries, or behavior in the environment. More concerted efforts to monitor pharmaceutical concentrations over time in aquatic ecosystems may help to resolve environmental drivers of their concentration and improve our ability to predict them.

KEYWORDS
concentration-discharge, nitrogen, pharmaceuticals and personal care products, phosphorus, random forest

INTRODUCTION

The link between excess nutrients and water quality issues has long been recognized. Excess nutrients in aquatic ecosystems contribute to eutrophication, harmful algal blooms, hypoxia, and associated loss of habitat and biodiversity (e.g., Carpenter, 2005; Galloway et al., 2003). In contrast, the impacts of emerging contaminants have been

appreciated only relatively recently. Mounting evidence shows that pharmaceuticals and personal care products, one broad category of emerging contaminants, can disrupt the reproductive and endocrine anatomy and physiology of aquatic organisms (e.g., Bergeron et al., 1999; Flammarion et al., 2000; Thorpe et al., 2001), fish and invertebrate behavior (e.g., Brodin et al., 2013; Reisinger et al., 2021), and metabolism and community composition of aquatic biofilm communities (Drury et al., 2013; Rosi et al., 2018; Rosi-Marshall et al., 2013; Rosi-Marshall & Royer, 2012). Concentrations of these synthetic chemicals in the environment are usually below thresholds for direct, acute toxicity, but they interfere with multiple ecological processes (Richmond et al., 2017) and their ubiquity in ecosystems across the world makes them agents of global change (Bernhardt et al., 2017).

Pharmaceuticals and personal care products enter aquatic ecosystems via treated and untreated wastewater from humans and domestic animals (Bradley et al., 2017; Ebele et al., 2017; Kolpin et al., 2002). Treated effluent from wastewater treatment plants is a well-studied point source of pharmaceutical pollution to urban streams (e.g., Fairbairn et al., 2016; Yu et al., 2006; Zhi et al., 2020). However, the types and amounts of individual pharmaceutical compounds in treated as compared with untreated wastewater are likely to differ (Fork et al., 2021). Leaks of untreated sewage during transport to treatment plants through aging subsurface pipes are a growing concern and a non-point source of pharmaceuticals to shallow groundwater and streams (Damashek et al., 2022; Roehrdanz et al., 2017; Sridhar & Parimalarenganayaki, 2024; Vystavna et al., 2018). Further, acute sewer infrastructure failures (such as combined sewer overflows [CSOs] and sanitary sewer overflows [SSOs]) discharge untreated wastewater and its associated load of pharmaceuticals directly to waterways (Reisinger et al., 2019). In urban streams that do not receive treated wastewater effluent, untreated wastewater from leaks and failures of sewage infrastructure may be a dominant source of pharmaceutical pollution.

Despite the mounting evidence that emerging contaminants negatively impact aquatic ecosystems, collecting and analyzing water samples, particularly for complex organic molecules like pharmaceuticals and other emerging contaminants, can be prohibitively expensive. As such, establishing predictive relationships between easier-to-monitor parameters that describe water quality or watershed conditions and the hard-to-monitor parameters of interest can make estimating and forecasting the amounts of emerging contaminants in aquatic systems more feasible. Advances in machine learning methods have led to the development of powerful and accurate models for estimating hard-to-monitor water quality parameters. For example, harmful algal blooms, which produce toxins (e.g., microcystin) that harm and kill a range of animals, have been accurately predicted using relatively inexpensive sensor measurements of water temperature, specific conductance, pH, dissolved oxygen, and turbidity (Recknagel et al., 2014). Concentrations of calcium and aluminum, which cannot be directly sensed in situ, can be accurately estimated using sensor measurements of fluorescent dissolved organic matter, pH, and specific conductance (Green et al., 2021). Similarly, predicting the concentrations of pharmaceuticals from routinely monitored parameters would allow for a more comprehensive understanding of the potential dangers of these contaminants to humans and ecosystems.

Using unique datasets from the Baltimore Ecosystem Study (BES) that describe 20 years of weekly water chemistry and one year of weekly pharmaceutical concentrations, we asked whether data about environmental conditions (stream discharge, land cover, SSOs in the watershed, etc.) and commonly measured water quality parameters (Cl, SO_4^{3-}, pH, temperature, etc.) could satisfactorily predict stream contaminant (nutrients and pharmaceuticals) concentrations. We used random forest (RF) models to predict whether concentrations of these contaminants were above or below environmentally relevant thresholds as well as the measured concentration. We developed two sets of RF models: one set to predict contaminant observations over time at the watershed outlet alone and another to predict over time and across subwatersheds that spanned an urban development gradient. Importantly, the streams in the BES do not receive treated wastewater effluent, and the system has separate sanitary and storm sewer systems, so the main source of pharmaceuticals is likely from leaks or overflows from sanitary sewers. We predicted that:

1. At higher stream discharge (Q), point sources (i.e., discrete leaks from aged or damage subsurface sewage infrastructure) are diluted, so Q will be an important predictor in models for both nutrients and pharmaceuticals.
2. Because nutrients and emerging contaminants share a common source (leaking sewage infrastructure), nutrient concentrations will help explain variability in pharmaceutical concentrations.
3. Because leaking sewage is likely to be an important source of both nutrients and emerging contaminants to streams, SSO occurrence/volume will be an important predictor in models for both types of contaminants within and among sampling sites.
4. Among sites, indices of urban development (e.g., impervious surface cover, population density) will be important predictors in models for both nutrients and pharmaceuticals.

METHODS

Study site

The BES (baltimoreecosystemstudy.org) core stream sites have been sampled weekly since 1999 and are described in detail elsewhere (Bettez et al., 2015; Groffman et al., 2004; Reisinger et al., 2019). The BES core stream sites are arranged primarily along Gwynns Falls and its tributaries in Baltimore City and County, Maryland, USA (Appendix S1: Figure S1). These sites have nested subwatersheds that range in area, impervious surface cover, and population density, from a small suburban watershed at the most upstream site (GFGL) to the highly urbanized context of the Gwynns Falls outlet (GFCP; Table 1). In addition to the sites within the Gwynns Falls watershed, BES core stream sites also include a forested reference watershed (POBR) and an exurban watershed (BARN) outside the Gwynns Falls watershed to the northeast (Table 1). Procedures for estimating watershed population densities are described by Fork and Locke (2020). Briefly, we intersected watershed polygons with census block polygons and used the proportion of the area of each census block within the watershed to estimate the proportion of that block's population that lived in the watershed. For example, if 40% of a census block intersected a watershed and the whole block had a population of 10 people, we assumed four people from that block lived within the watershed. The overall watershed population density is a sum of the total estimated population across all census blocks that intersected the watershed, divided by total watershed area.

TABLE 1 Watershed characteristics for Baltimore Ecosystem Study subwatersheds used in this study, ordered by percent impervious surface cover.

Site	Area (km^2)	% impervious surface cover	Estimated population density (people km^{-2})
MCDN	0.0746	0	9
POBR	0.353	0	39
BARN	3.86	1.09	125
GFGB	10.6	17.23	1651
GFGL	0.834	18.97	1207
GFVN	84.3	20.09	1435
GFCP	165	27.53	1950
DRKR	14.3	39.82	1141

Sample collection and analysis

We used data from weekly water samples of nutrients (collected from 2001 to 2018) and pharmaceuticals (collected 2 November 2017 through 15 November 2018). The methods for the collection and analysis of nutrient and pharmaceutical samples have been described in detail elsewhere (Fork et al., 2021; Groffman et al., 2004). Briefly, grab samples for water chemistry were collected at or near USGS gaging stations by wading. Samples were collected approximately 15 cm below the water surface in the center of the channel or at weir notches in shallow headwaters. Samples for nitrate were filtered in the field using a syringe and GF/A glass fiber filter (Whatman, Maidstone, Kent, UK) plus a 0.45-μm-pore nylon filter. Samples for total nutrients and for pharmaceuticals were unfiltered. Nutrient samples were collected in 150-mL low-density polyethylene Nalgene bottles, and pharmaceutical samples were collected in 5-mL polypropylene vials (Corning 430663). Samples were stored on ice in the dark until returning to the laboratory at the University of Maryland, Baltimore County, where they were bagged by the sampling site and frozen at −20°C. Periodically, frozen samples were shipped overnight to the Cary Institute of Ecosystem Studies and stored frozen.

Nutrient samples were analyzed on a Dionex LC20 series (Dionex, Sunnyvale, CA, USA) ion chromatograph following digestion for total nutrient samples. Pharmaceutical samples were shipped to Umeå University, Sweden, where they were screened for concentrations of 92 pharmaceuticals using a liquid chromatography mass spectrometry UHPLC system connected to a TSQ Quantiva triple quadrupole mass spectrometer (Thermo Scientific). Detailed descriptions of analysis and quality assurance/quality control for pharmaceutical samples are available elsewhere (Fork et al., 2021; Lindberg et al., 2014). Total pharmaceutical concentration in a sample was calculated as the summed concentrations of any of the target compounds ($n = 92$) quantifiable in the sample.

Data analysis

Data preprocessing

Streamflow data were accessed from the US Geological Survey for each BES core stream site using the dataRetrieval package for R (DeCicco et al., 2023). We estimated the instantaneous flow at the time of sampling by taking the mean of 5- or 15-min stream discharge during a 20-min window centered on the reported sampling time. For samples missing a reported sampling time ($n = 1243$ of 7785 total samples, or about 16% of

samples), we estimated the sampling time as the mean of all reported sampling times for that site, as the BES core sites were sampled in the same order at approximately the same time of day in each instance.

The volume and type (wet or dry conditions) of SSOs in Baltimore City and County are reported by the Maryland Department of the Environment (2020). We used the reported spatial information to identify reported SSOs that occurred within the watersheds of BES core stream sites in the day or week preceding sample collection. These data were used as potential predictors of nutrients and pharmaceuticals for the 2018 water year only; the records are not complete for the period from 2001 to2018. For the purposes of our analysis, we use water year (here, November 1–October 31) instead of calendar year (January 1–December 31) because water years tend to minimize year-to-year storage in the watershed and therefore provide clearer annual analyses.

Erroneous data in the records (water temperatures greater than 100°C, pH less than 1 or greater than 14, and turbidity greater than 10,000 NTU) were replaced by "NA" before analysis. Day of year was also included in models following sin-transformation to encode this cyclical variable appropriately for detecting possible seasonal patterns.

Concentration-discharge and SSO analysis

First, we assessed the concentration-discharge (C-Q) relationships for total nutrients (total nitrogen [TN] and total phosphorus [TP]) as well as total pharmaceuticals. All data were log-transformed before using simple least squares linear regression. We also assessed the simple linear relationship between log-transformed total nutrient concentrations and the log-transformed total volume of SSOs reported in the watershed for the week preceding sampling using the same approach. Likewise, we assessed the relationship between log-transformed total pharmaceutical concentrations and log-transformed SSO volume.

RF modeling

We used the RF (Breiman, 2001) algorithm to predict continuous variables (TN, TP, and total pharmaceutical concentrations) and categorical variables (detection of trimethoprim and threshold nutrient concentrations, below). RF models create a series of trees that predict the dependent variable. Each node of a tree splits a random subset of the data according to a random permutation of independent variables, with the remaining data used to test the performance of the individual trees. The importance of each independent variable is calculated by comparing the performance of trees with and without that variable. The final prediction is the average prediction of the individual trees, with the overall performance calculated using the error rate across all trees.

We chose RF because it is robust to correlation among predictors, can represent nonlinear patterns, and reduces the risk of overfitting to training data. RF models have been used successfully for gap-filling and prediction of solute concentrations and biogeochemical fluxes (Green et al., 2021; Kim et al., 2020; Olson & Hawkins, 2012; Regier et al., 2023; Rodriguez-Galiano et al., 2014). We used the randomForest package (Liaw & Wiener, 2002) in R version 4.1.0 (R Development Core Team, 2021) to build RF models for our data, with five variables tried per split in an individual tree and using 100 trees per model, in accordance with recommendations from Regier et al. (2023). Eighty percent of the data were used for training, with the remaining 20% used to assess and validate models. Missing values in the predictors were imputed as the median (for continuous variables) or the mode (for categorical variables).

Predictors included in RF models

After compiling the full list of potential predictor variables for models, we omitted variables with observations at fewer than 50% of the sampling points. After log-transforming variables with highly skewed distributions, we examined the pairwise correlations (Pearson's r; Appendix S1: Tables S1 and S2). For each model, we omitted highly correlated variables ($r > 0.7$; except that the wet vs. dry information was retained for corresponding SSO volume data even when these two variables were highly correlated) to arrive at a final list of predictors to include (Appendix S1: Tables S3 and S4). For models of nutrient concentrations, we omitted predictors that included the same type of nutrient (e.g., for models predicting TN, we omitted nitrate concentration [NO_3^-] from the predictors included as model input). For models used to predict chemistry across multiple subwatersheds, we normalized stream discharge by dividing the mean instantaneous stream discharge from the US Geological Survey by watershed area. These and all other analyses were performed in the R environment (version 4.1.0, R Development Core Team 2021).

Thresholds and categorical response variables

In addition to modeling concentrations, we also used RF to predict when nitrate and TP concentrations exceeded environmentally relevant thresholds and the detection/non-detection of the antibiotic trimethoprim. In this case, RF predicts a classification of the sample as above/below

the threshold concentration or limit of quantification. These thresholds may be more useful for management actions, particularly if the approach performs better for such classification than for regression. We chose a threshold concentration of 1 mg N L^{-1} for nitrate because this is the threshold used by Maryland Department of Natural Resources to define "unnaturally elevated nitrate levels" (Department of Natural Resources, n.d.). For TP, we used a threshold of 40 μg L^{-1} because the US EPA reports this value as the upper limit of an "acceptable range for TP" (US EPA, 2009).

We used the detection of the antibiotic trimethoprim as a categorical response for pharmaceuticals. This compound was the most frequently detected of 92 compounds screened, found in 137 of 371 total samples (Fork et al., 2021). Furthermore, trimethoprim is relatively hydrophilic (logP = 0.91; Kim et al., 2023), making it less subject to removal from the water column by sorption to sediments. In this way, the physical behavior of trimethoprim in the aquatic environment may be similar to that of nitrate. Relatively balanced observations of detection and non-detection, as well as a low affinity for sediment, make this a good compound for our modeling approach.

In total, we created 20 different RF models (Figure 1). For data from the 2018 water year ("WY2018" hereafter), we created six models for data from the watershed outlet: three models predicted concentrations of TN, TP, and total pharmaceuticals, respectively, and three models predicted categorical responses (NO_3^- concentration above or below 1 mg N L^{-1}, TP concentration above or below 40 μg L^{-1}, and whether trimethoprim was detected). Each of these models used 45 samples. We also created a similar set of six RF models for WY2018 using data from across the BES subwatersheds ($n = 340$ samples). In addition, we created two RF models for nutrient data over the full water chemistry record (2001–2018): models predicting TN and TP concentrations at the watershed outlet only ($n = 903$ samples) and across subwatersheds ($n = 6917$ samples); and models predicting whether NO_3^- concentration was above or below 1 mg N L^{-1} and whether TP concentration was above or below 40 μg L^{-1} for both the watershed outlet and across subwatersheds.

We evaluated the performance of RF models using information about training data and validation data. For models that predicted nutrient or pharmaceutical concentrations, we used the mean percent of variance explained by the model in the training dataset (calculated as 1 − mean square error divided by the variance in the response) and the Nash-Sutcliffe efficiency (NSE)

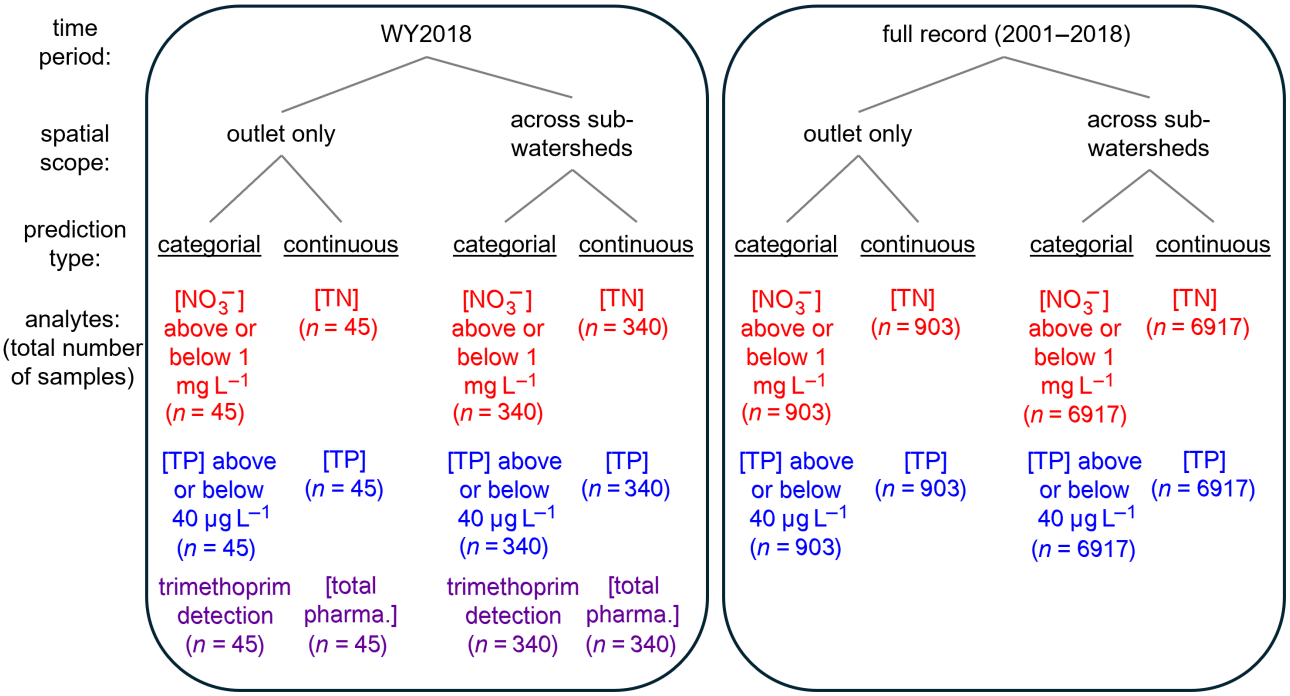


FIGURE 1 Depiction of data used for the 20 random forest models created as part of this study. Twelve models were built using data from the 2018 water year (WY2018) only: six models for the watershed outlet only and six for sites across multiple Baltimore Ecosystem Study (BES) subwatersheds. These included categorical models for predicting whether nutrient (nitrate [NO_3^-] and total phosphorus [TP]) and pharmaceutical (trimethoprim) concentrations were above an environmentally or analytically relevant threshold. We also included models with continuous output for predicting concentrations of total nitrogen (TN), TP, and total pharmaceuticals (total pharma.). Eight models were built using the full data record for nutrients (2001–2018) including the categorical and continuous models at the outlet along and across subwatersheds.

calculated for the validation dataset (using the package hydroGOF, Zambrano-Bigiarini, 2024). The NSE describes the variance of predicted concentrations and measured concentrations around the 1:1 line. For categorical models, we assessed model performance using the mean error rate for the model in the training dataset and the percentage of miscategorized samples in the validation dataset.

RESULTS

Nutrients at the watershed outlet

Over the long term (2001–2018), TN ranged from 0.57 to 6.61 mg L^{-1} and TP ranged from 1.3 to 645 with a mean of 30.0 μg L^{-1} (Appendix S1: Figure S2). Over WY2018, TN concentrations ranged from 0.59 to 2.61 mg L^{-1}, with a mean of 1.33 mg L^{-1} (Figure 2a). Over the first half of WY2018, TP concentrations were always below 20 μg L^{-1}, with a mean of 6.4 μg L^{-1}. During the second half of WY2018, however, we found higher, more variable TP concentrations that ranged from 5.8 to 253 μg $L,^{-1}$ with a mean of 41.7 μg L^{-1} (Figure 2b).

Relationships of nutrients to Q and SSOs

Over the full record (2001–2018), the C-Q relationship for TN was not significant ($p = 0.54$), indicating a chemostatic relationship over the long term. For TP, we found a significant positive C-Q relationship ($p < 0.0001$ and $R^2 = 0.09$), indicating enrichment of TP at high flows (Appendix S1: Figure S2). During WY2018, weekly grab samples were taken at conditions that spanned nearly the entire range of flow over the year (Fork et al., 2021). Discharge at the time of sampling was positively related to both TN and TP for the 2018 water year, indicating an enriching relationship for both nutrients (Figure 2c,d). For TN, the positive C-Q relationship is relatively weak ($p = 0.03$, $R^2 = 0.07$) and the positive C-Q relationship for TP is considerably stronger ($p < 0.0001$, $R^2 = 0.54$). SSO volume in the preceding week did not predict either TN or TP for 2018 (for TN: $p = 0.79$; for TP: $p = 0.23$; Figure 2e,f).

Modeling of nutrient concentrations and thresholds

Over the full record of water chemistry (2001–2018), the model for TN explained 36.0% of the observed variation in concentrations in the training dataset, and the NSE comparing the relationship of the observed and predicted validation data to the 1:1 line was 0.508. The sulfate concentration was the most important predictor in the long-term TN concentration model for the watershed outlet (Appendix S1: Figure S3). The long-term model for TP concentration explained 49.5% of the observed variation in concentrations in the training dataset, and the NSE for validation data was 0.741. Here, TN concentration and log-transformed chloride concentration were the most important predictors in the model (Appendix S1: Figure S3).

For NO_3^- over the full record, the model for predicting whether nitrate concentrations were above or below a threshold of 1 mg N L^{-1} had an error rate of 16.0% for training data and miscategorized 19.0% of observations in the validation data. Log-transformed chloride and sulfate concentrations were the most important predictors in this model. For TP, our long-term threshold model had an error rate of 13.9% for the training data but miscategorized only 6.90% of the validation data. In this model, TN and sulfate concentrations were the most important predictors (Appendix S1: Figure S3).

In WY2018, RF models predicting total nutrient concentrations at the Gwynns Falls watershed outlet performed poorly for TN and fairly well for TP. The model for TN concentration during WY2018 explained less than 0% of the observed variation in TN concentration in the training data, and the NSE for the validation data was very low (−0.422; Figure 3a,b). In contrast, the model for WY2018 at the watershed outlet explained 59.6% of the variation in TP concentration of the training data and had an NSE of 0.833 for the validation data, with temperature and log-transformed chloride concentration as the most important predictors (Figure 3c,d).

The WY2018 threshold models performed similarly to the long-term models for the watershed outlet. The model for predicting whether nitrate concentrations were above or below a threshold of 1 mg N L^{-1} had an error rate of 19.4% for the training data and miscategorized 25% of the validation data. In this model, the volume and types (wet vs. dry weather) of SSOs in the week preceding sampling were the most important predictors (Figure 3e,f). The model for predicting whether TP concentrations were above a threshold of 40 μg L^{-1} had an error rate of 2.78% for the training data and miscategorized none (0%) of the observations in the validation dataset. For the TP threshold model, pH and log-transformed chloride concentration were the most important predictors (Figure 3g,h).

Nutrients across subwatersheds

C-Q across sites

Over the long-term record of water chemistry, the majority of sites showed significant C-Q relationships for TN

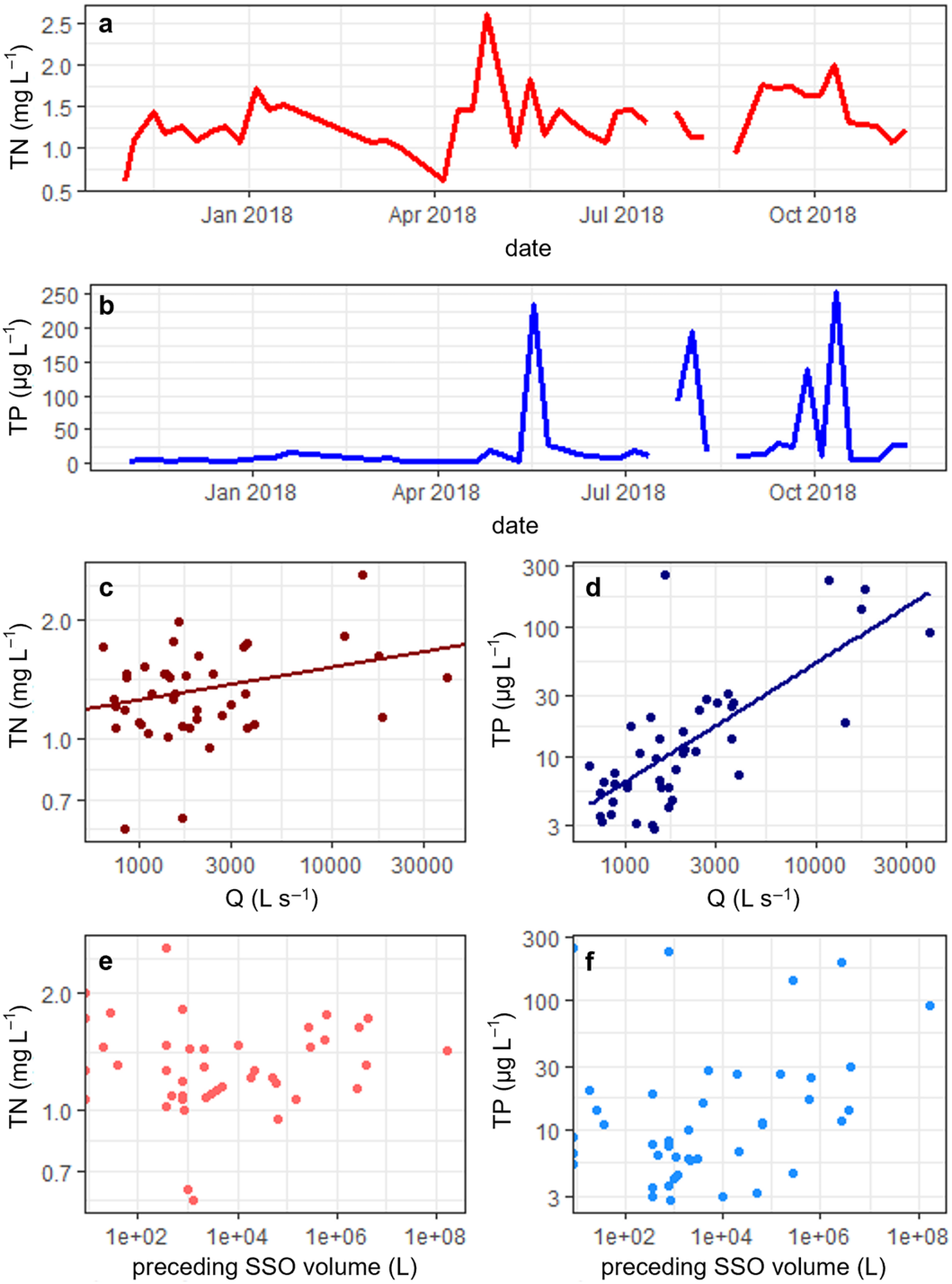


FIGURE 2 Total nitrogen (TN) and total phosphorus (TP) at the watershed outlet (GFCP). (a, b) We show concentrations over time for water year 2018 (c, d) concentrations versus stream discharge (Q) at the time of sampling, and (e, f) concentrations versus the total volume of sanitary sewer overflows (SSO) that occurred in the watershed during the seven days preceding the sample.

and TP, but the direction (i.e., enriching vs. diluting) differed. Specifically, long-term C-Q relationships for TP were positive (enriching) at two of the upstream sites along the Gwynns Falls mainstem (GFVN: $p < 0.0001$, $R^2 = 0.20$; GFGB: $p < 0.0001$, $R^2 = 0.16$). While the C-Q relationship for TP was negative (diluting) at the furthest upstream site (GFGL) and agricultural subwatershed (MCDN), these relationships were considerably weaker than the C-Q relationships observed at other Gwynns Falls sites (BARN: $p < 0.0001$, $R^2 = 0.04$; MCDN: $p < 0.0001$, $R^2 = 0.02$). We found a weak but positive relationship between TP and Q at the exurban site (BARN: $p = 0.0001$, $R^2 = 0.02$), while

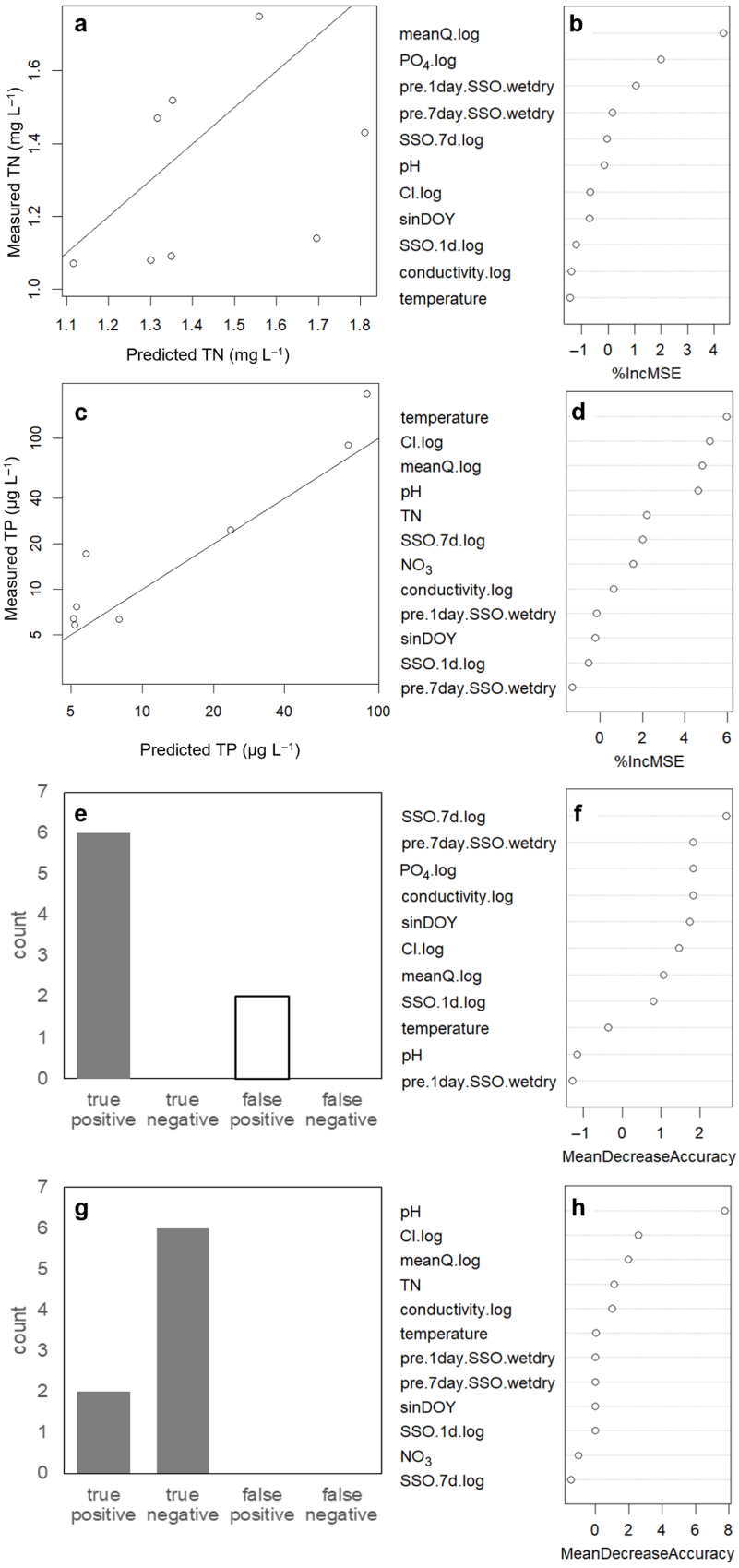


FIGURE 3 Legend on next page.

the forested reference (POBR) and highly urbanized (DRKR) watersheds did not have significant C-Q relationships (chemostasis) for TP over the long-term (POBR: $p = 0.69$; DRKR: $p = 0.54$).

For TN, we calculated weak but significant negative (diluting) C-Q relationships at two of the upstream sites along the Gwynns Falls mainstem and in the forested reference (GFVN: $p = 0.04$, $R^2 = 0.004$; GFGB: $p < 0.0001$, $R^2 = 0.27$; POBR: $p < 0.0001$, $R^2 = 0.03$). In contrast, we found weak but significant positive (enriching) C-Q relationships for TN over the long term at the furthest upstream Gwynns Falls site (GFGL), the exurban watershed (BARN), the highly urbanized watershed (DRKR), and the agricultural subwatershed (MCDN) (GFGL: $p = 0.02$, $R^2 = 0.006$; BARN: $p < 0.0001$, $R^2 = 0.03$; DRKR: $p = 0.05$, $R^2 = 0.004$; MCDN: $p = 0.0006$, $R^2 = 0.01$).

Like the watershed outlet, two of the upstream sites along the Gwynns Falls mainstem had significant positive C-Q relationships for TP in WY 2018 (GFVN: $p = 0.00016$, $R^2 = 0.27$; GFGB: $p < 0.0001$, $R^2 = 0.43$), but the furthest upstream site did not show a significant C-Q relationship for TP during this time period (GFGL: $p = 0.36$). The nearby exurban site (BARN) also had a positive C-Q relationship for TP ($p = 0.03$, $R^2 = 0.07$), while the forested reference site (POBR) did not show a significant relationship ($p = 0.12$). Unlike the watershed outlet, the other sites along the Gwynns Falls mainstem all had slightly diluting (i.e., negative) C-Q relationships for TN during WY2018 (GFVN: $p = 0.018$, $R^2 = 0.11$; GFGB: $p < 0.0001$, $R^2 = 0.64$; GFGL: $p = 0.0002$, $R^2 = 0.27$). The exurban site also had a diluting C-Q relationship for TN in WY 2018 (BARN: $p < 0.0001$, $R^2 = 0.41$), while the forested reference site (POBR) showed no significant relationship ($p = 0.12$). Concentration–discharge relationships for WY2018 were not assessed for the agricultural subwatershed (MCDN) and the highly urbanized watershed (DRKR) because of missing nutrient data.

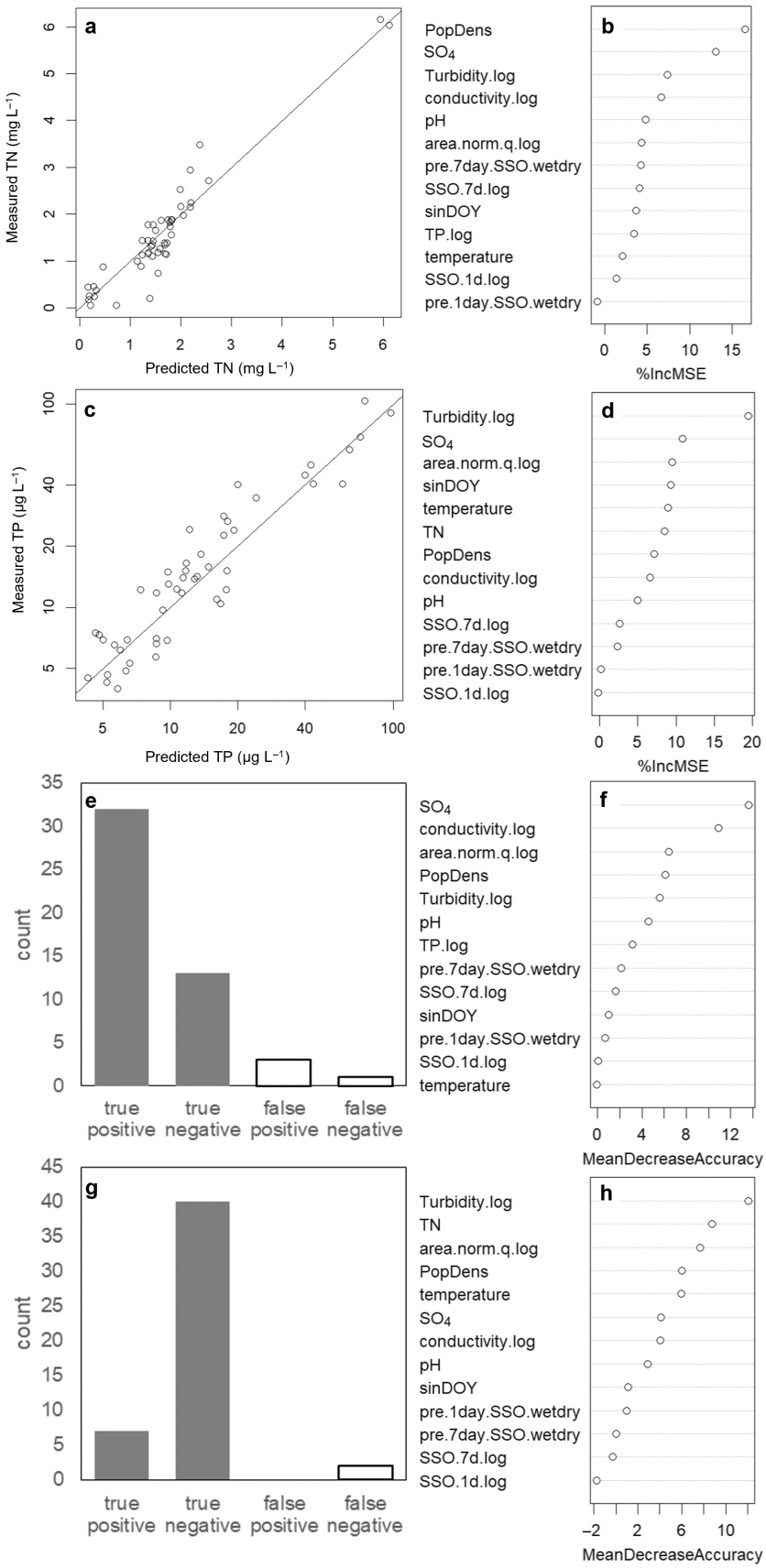
RF modeling

Over the long-term water chemistry record, the RF model explained 92.8% of the variation in TN concentrations among sites in the training dataset, and the observed and predicted data in the validation set had an NSE of 0.933. Population density in the subwatershed was the most important predictor (Appendix S1: Figure S4). The model for long-term TP across subwatersheds explained 67.4% of the observed variation in the training data concentrations across sites from 2001 through 2018, and the validation dataset showed an NSE of 0.744, with turbidity as the most important predictor (Appendix S1: Figure S4).

RF models also accurately predicted whether nutrient concentrations were above or below a given threshold across BES subwatersheds, and models for predicting NO_3^- concentrations above/below 1 mg N L^{-1} and TP concentrations above/below 40 μg L^{-1} across the BES core stream sites performed similarly to one another. For nitrate, the model had an error rate of 9.26% for training data and miscategorized 10.9% of validation data, with sulfate concentration as the most important predictor (Appendix S1: Figure S4). The model for TP had an error rate of 10.0% for the training data and miscategorized 10.6% of validation data. Turbidity was the most important predictor of TP thresholds over the full record (Appendix S1: Figure S4).

Modeling results were similar for WY2018 alone. The RF model explained 90.2% of the observed variation in training data TN concentrations across sites. The NSE comparing observed and predicted TN concentrations from the validation data to the 1:1 line was 0.899. Population density for the subwatershed of the sampling site and sulfate concentration were the most important predictors (Figure 4a, b). Similarly, the WY2018 model across subwatersheds described 76.8% of the variation in TP concentrations in the training data and had an NSE of 0.864 for the validation data, with turbidity and sulfate concentration as the most important predictors (Figure 4c,d).

FIGURE 3 Observed versus modeled nutrient data and most important predictors in random forest models for the watershed outlet in water year 2018. (a) For total nitrogen ("TN") concentration at the Gwynns Falls outlet, the model does not accurately predict measured concentrations in the validation data (line shows 1:1 relationship; Nash-Sutcliffe efficiency [NSE] = −0.422). (b) In this model, log-transformed mean discharge at the time of sampling ("meanQ.log") and log-transformed orthophosphate concentration ("PO4.log") as the most important predictors (as measured by the percent increase in mean squared error when a predictor is not included in a model ["% IncMSE"]). (c) The model for total phosphorus ("TP") has much better correspondence between modeled and observed concentrations in the validation data (NSE = 0.833) with (d) water temperature and log-transformed chloride concentrations ("Cl.log") as the most important predictors. The models were also generally accurate in predicting whether nutrient concentrations were above or below a given threshold: (e) the model for NO_3^- miscategorized 25% of samples in the validation dataset as having concentrations above 1 mg N L^{-1} when measured concentrations were below this threshold (i.e., "false positive"). (f) Here, the type (wet vs. dry weather; "pre.7 day.SSO.wetdry") and log-transformed volume of sanitary sewer overflows ("SSO.7d.log") in the preceding 7 days were the most important predictors. (g) For TP, the model did not miscategorize any observations in the validation data, with (h) pH and Cl.log as the most important predictors. Full descriptions of predictors (b, d, f, h) are found in Appendix S1: Table S3.



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For NO_3^- thresholds, the WY2018 model had a 6.62% error rate in predicting concentrations above versus below 1 mg N L^{-1} for training data across subwatersheds and miscategorized 8.16% of the observations in the validation data. In this model, sulfate concentration and conductivity were the most important predictors (Figure 4e,f). For TP, the model had a 4.78% error rate in predicting concentrations above versus below 40 μg L^{-1} for the training data and miscategorized 4.08% of TP observations in the validation data, with turbidity and TN concentrations being the most important predictors (Figure 4g,h).

Pharmaceutical concentration and detection across subwatersheds

Relationships to Q and SSOs

Discharge was not a good predictor of total pharmaceutical concentration at the watershed outlet (GFCP) over WY2018 ($p = 0.89$; Figure 5). Results were similar for the majority of other subwatersheds in the Gwynns Falls watershed (GFVN: $p = 0.17$; GFGL: $p = 0.80$; MCDN: $p = 0.57$; DRKR: 0.95) and for the forested reference site (POBR: $p = 0.68$). However, two sites exhibited significant negative (diluting) C-Q relationships for total pharmaceuticals: the exurban watershed (BARN: $p < 0.0001$, $R^2 = 0.31$) and an upstream site along the Gwynns Falls mainstem (GFGB: $p = 0.05$, $R^2 = 0.06$).

SSO volume in the preceding week was a similarly poor predictor of total pharmaceutical concentration at the watershed outlet ($p = 0.64$; Figure 5). Only one of the 43 recorded SSOs occurred within a monitored subwatershed of Gwynns Falls, so we presume the importance of SSOs at other sites is low.

RF modeling

In general, RF models performed poorly for the prediction of total pharmaceutical concentration and trimethoprim detection. Specifically, the model for total pharmaceutical concentration at the watershed outlet explained less than 0% of the observed variance over water year 2018 in the training data, with sin-transformed day of year as the most important predictor (Figure 6a,b). The predicted and observed total pharmaceutical concentrations in the validation dataset for this model did not lie near the 1:1 line (NSE = 0.172), further indicating poor model performance. The model for trimethoprim detection at the watershed outlet had an error rate of 69.4% in the training data and miscategorized 62.5% of observations in the validation data, performing worse than random chance and including the type and volume of SSOs in the preceding week as the most important predictors (Figure 6c,d). Models that included data across subwatersheds performed somewhat better: The model for total pharmaceutical concentration across subwatersheds explained 17.8% of the variance observed in the training data and had an NSE of 0.101 for the validation data, with sinDOY again the most important predictor (Figure 6e,f). Across all BES subwatersheds, the model predicting the detection of trimethoprim had a 38.2% error rate for the training data and miscategorized 40.8% of observations in the validation data, with the type of SSOs (wet vs. dry) in the preceding week and the sample conductivity as the most important predictors (Figure 6g,h).

DISCUSSION

Our results from streams in Baltimore, Maryland, demonstrate differences in the controls on, and therefore the predictability of, traditional (i.e., nutrients) versus emerging contaminants (pharmaceuticals). At the watershed outlet, TP concentrations and thresholds were accurately predicted from routinely monitored water quality parameters (specifically water temperature, pH, TN, sulfate, and chloride concentrations), even when parameters highly correlated with TP (turbidity and phosphate concentrations) were omitted. Predictions of TN and nitrate were less accurate at the watershed outlet, whether assessed for a single year (WY2018) or over the full water

FIGURE 4 Observed versus modeled nutrient data and most important predictors in random forest models across BES subwatersheds during the 2018 water year. (a) For total nitrogen ("TN") concentration, the modeled and observed data in the validation dataset agree well (line shows 1:1 relationship; Nash-Sutcliffe efficiency [NSE] = 0.899) with (b) population density for people living in the watershed of the sampling site ("PopDens") the sulfate concentration ("SO_4") as the most important predictors (as measured by the percent increase in mean squared error when a predictor is not included in a model ["%IncMSE"]). Likewise, (c) for total phosphorus ("TP") there is good correspondence between modeled and observed concentrations in the validation data (NSE = 0.864), with (d) log-transformed turbidity ("Turbidity.log") and SO_4 as the most important predictors. The models were also accurate in predicting whether nutrient concentrations were above or below a given threshold: (e) the model for nitrate miscategorized 8.16% of the validation data, with (f) SO_4 and log-transformed specific conductance ("conductivity.log") as the most important predictors. (g) For TP, the model miscategorized 4.08% of observations in the validation data, with (h) Turbidity.log and TN as the most important predictors. Full descriptions of predictors (b, d, f, h) are found in Appendix S1: Table S3.

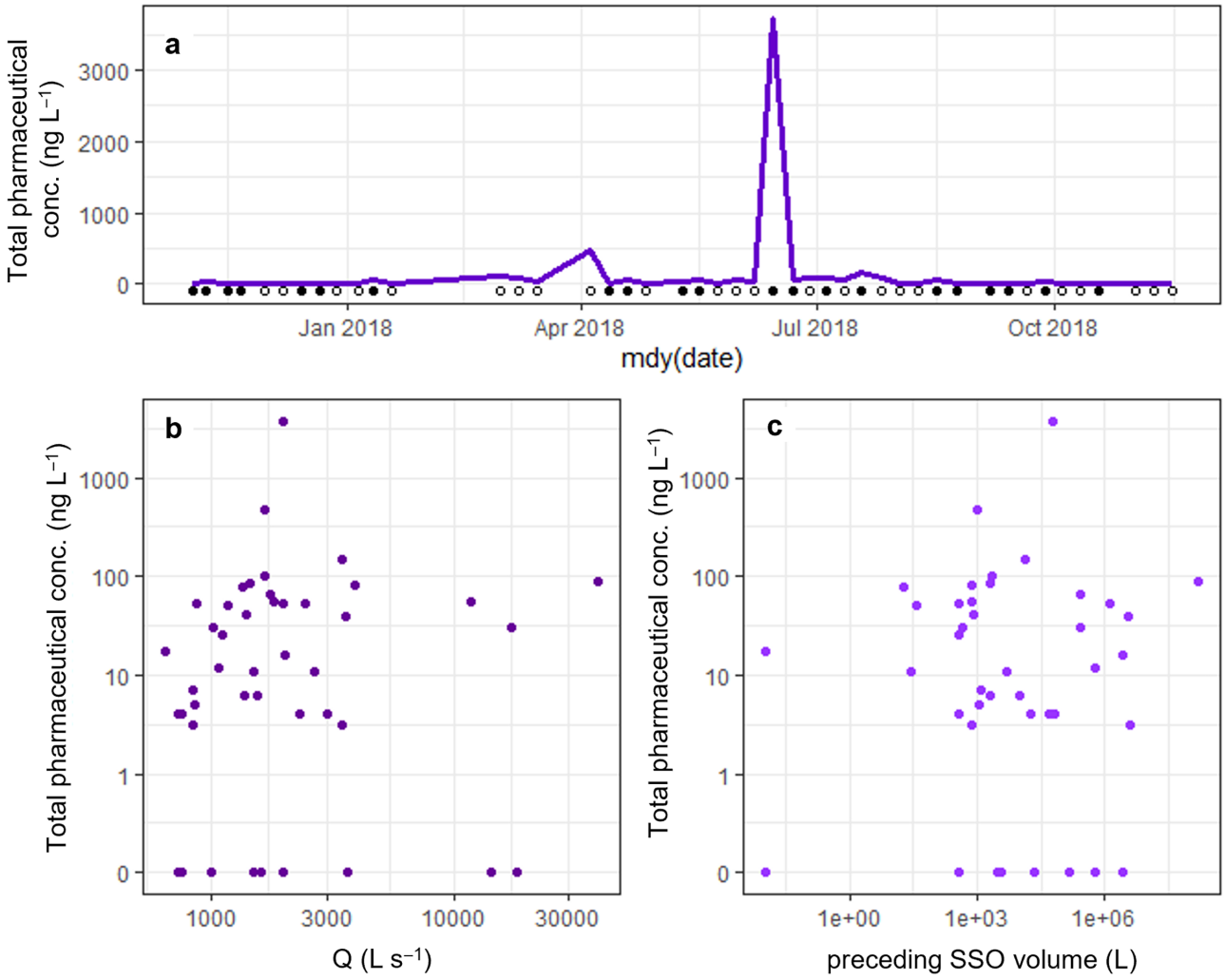

FIGURE 5 Total pharmaceutical concentration and relationship to stream discharge (Q) and sanitary sewer overflows (SSO) at the watershed outlet (GFCP). We show (a) total pharmaceutical concentrations over time for water year 2018 (purple line) as well as individual samples in which the compound trimethoprim was detected (filled symbols) and not detected (open symbols). We also show (b) the concentration-discharge relationship for total pharmaceuticals and (c) total pharmaceutical concentrations versus the total volume of SSOs that occurred in the watershed during the seven days preceding the sample.

chemistry record (2001–2018). Models for TN concentrations at the watershed outlet explained less than 40% of the variance in observed concentrations for the training data used to build the model, in contrast to nearly 50% or more variance explained for TP concentration models. Similarly, models predicting whether NO_3^- concentrations were above the environmentally relevant threshold of 1 mg N L^{-1} did have error rates >15% for the training data and similar rates of mis-categorization of validation data, while models for TP thresholds had error rates <15% for training data and mis-categorized less than 10% of observations in the validation data. However, when we expanded the models to predict across subwatersheds, the accuracy of models for N improved greatly, at least in part because variations in the watershed-scale population density helped to predict N variation among sites. However, we also note that there were a greater number of samples included in models that predicted across subwatersheds (Figure 1), which likely also played a role in improving the performance of these models relative to the models using data from the watershed outlet alone.

Models to predict total pharmaceutical concentrations and trimethoprim detection using the same input data always performed poorly, whether for the watershed outlet alone or across subwatersheds. Unlike nutrients, pharmaceutical concentrations do not show a coherent pattern with discharge (Figure 5b). At the watershed outlet, the model for trimethoprim detection performed worse than random chance, and the model for total pharmaceutical concentrations explained less than 0% of the variance in observed concentrations in the training data. Models across sites performed slightly better, but still

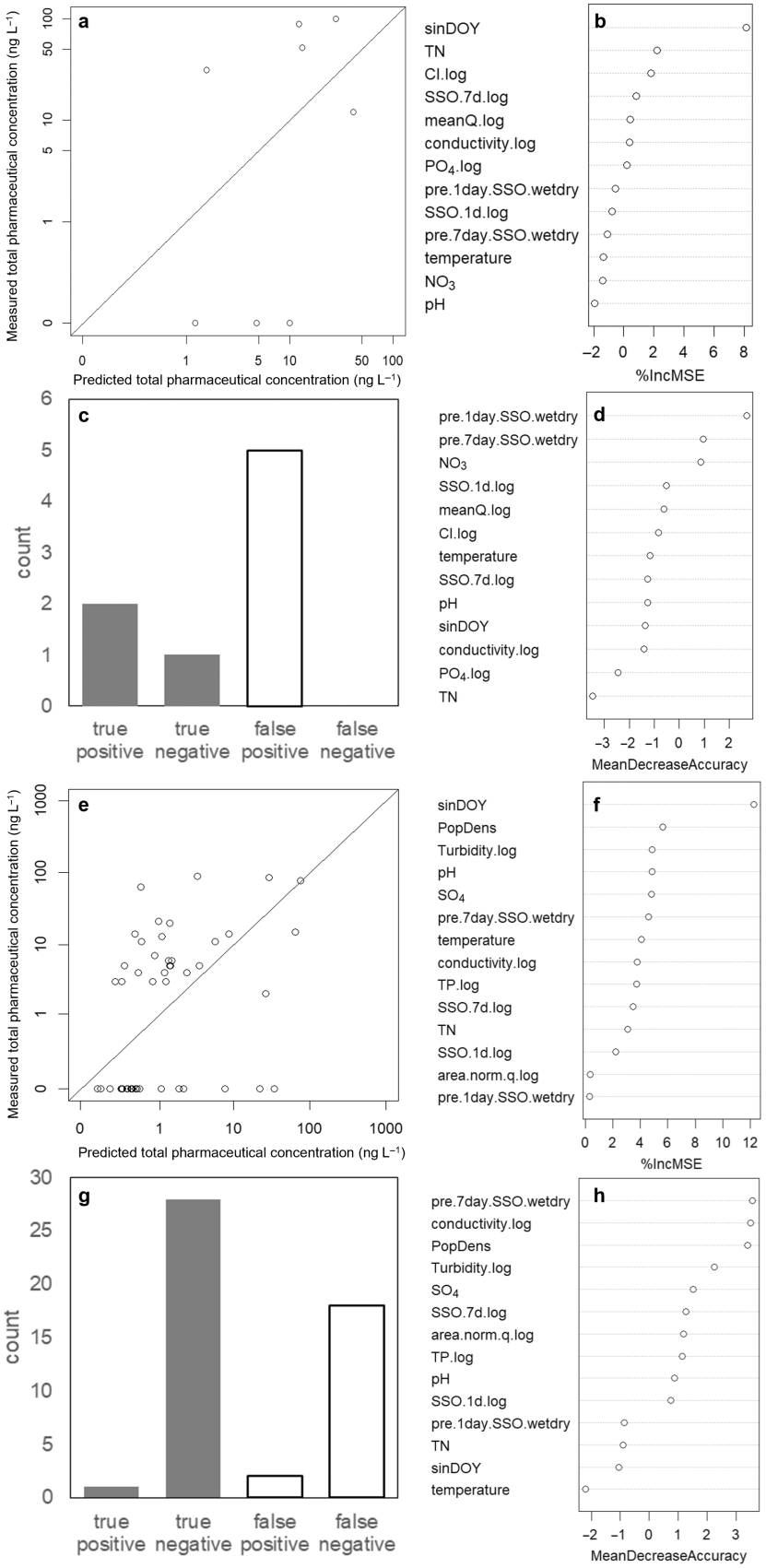

FIGURE 6 Legend on next page.

substantially worse than nutrient models. We note that, for all models in our analysis, the general agreement between evaluation of models using training data and validation data for a given model indicates that models were generally not influenced by overfitting to the training dataset.

We hypothesized that discharge would be an important predictor for nutrients and for pharmaceuticals. We found that discharge was a fairly important predictor of both TP and TN concentrations, showing a significant positive relationship with each constituent (Figure 2c,d) and being a relatively important predictor in RF models (Figures 2 and 3). In contrast, we did not find strong evidence that stream discharge was a good predictor of pharmaceutical concentrations. Only two of the eight BES sampling sites for different subwatersheds had significant but weak negative relationships between total pharmaceutical concentration and stream discharge. Further, discharge was not an important predictor of concentration or threshold behavior in RF models for pharmaceuticals, especially when comparing among subwatersheds (Figure 6).

We also hypothesized that SSOs would be important predictors for nutrients and for pharmaceuticals, but did not find consistent evidence for this. Neither total nutrient concentrations nor pharmaceutical concentrations showed significant relationships with the volume of SSOs in the week preceding sampling (Figures 2e,f and 5c). While SSO volume and type were useful predictors of nutrients in some models (specifically, nitrate threshold behavior at the watershed outlet; Figure 3f) and SSO type in the preceding day and week were important predictors of trimethoprim detection at the watershed outlet (Figure 6d), SSOs were not consistently important in our analysis, and the models for which they were important performed moderately to poorly. Further, SSOs were only reported in two of our study watersheds (GFCP, with 215 events in our analysis and GFVN, with 2 events), and primarily represent acute events, not any slower or smaller volume leaks that may be present in either centralized or on-site wastewater treatment systems. SSOs are the best quantitative estimate we have for sewage inputs to this watershed, and they do help to explain the annual mass balance of pharmaceuticals (Fork et al., 2021) and annual nitrate, phosphate, and TN loads (Reisinger et al., 2019). At finer timescales, however, SSOs do not seem to explain the dynamics of pharmaceutical concentrations in this urban stream network.

Across sites, we hypothesized that measures of urbanization (impervious surface cover, population density) would be important predictors in models for both nutrients and pharmaceuticals. These measures of urbanization were strongly correlated among watersheds in our study, so we chose to use population density as the measure of urbanization here. Previous work in the BES core stream sites has suggested a pattern between watershed population density and the concentration and detection rate of pharmaceuticals (Fork et al., 2021). As such, it is no surprise that population density was of moderate to high importance in models predicting total pharmaceutical concentration and trimethoprim detection across BES streams (Figure 6f,h). Likewise, the links between watershed urbanization and nutrient concentrations in urban streams are well documented (e.g., Groffman et al., 2004; Paul & Meyer, 2001; Walsh et al., 2005), so the moderate to high importance of population density in models of nutrients (Figure 4) is similarly unsurprising.

Finally, we hypothesized that nutrient concentrations would help to predict pharmaceutical concentrations. This hypothesis was not supported by our analysis. First, models for pharmaceuticals performed poorly, despite including nutrient concentrations as predictors. Second, nutrient concentrations were rarely important predictors even in these poorly performing models. In the RF models for total pharmaceutical concentrations, nutrient concentrations were of low to medium importance as predictors, surpassed by day of year (Figure 6b,f). This result suggests a lack of covariation between total

FIGURE 6 Observed versus modeled data for total pharmaceutical concentration and trimethoprim detection and the most important predictors in random forest models. (a) For total pharmaceutical concentration at the watershed outlet, the model does not accurately predict concentrations in the validation data (line shows 1:1 relationship; Nash-Sutcliffe efficiency [NSE] = 0.172), with (b) the sin-transformed day of year ("sinDOY") as the most important predictor (as measured by the percent increase in mean squared error when a predictor is not included in a model ["%IncMSE"]). (c) The model predicting detection of trimethoprim performs poorly, mis-categorizing 62.5% of samples in the validation dataset. (d) Here, the type (wet vs. dry weather) of sanitary sewer overflows in the preceding day and week ("pre.1 day.SSO.wetdry" and "pre.7 day.SSO.wetdry," respectively) were the most important predictors of trimethoprim detection. (e) Across subwatersheds, the model also performs poorly at predicting total pharmaceutical concentrations in the validation data (NSE = 0.101), with (f) sinDOY again the most important predictor. The model for trimethoprim using data from across subwatersheds performs somewhat better than random chance (g), mis-categorizing 40.8% of observations in the validation data, with pre.7 day.SSO.wetdry and log-transformed specific conductance ("conductivity.log") as the most important predictors (h). Full descriptions of predictors (b, d, f, h) are found in Appendix S1: Table S4.

pharmaceutical concentration and other water quality measures. Similarly, nutrient concentrations were generally not useful predictors of trimethoprim detection (Figure 6d,h). We hypothesized that nutrient and pharmaceutical concentrations would be related because we expected them to share common sources (namely human and pet waste). However, there are likely many more potential sources of nutrients in the urban landscape (e.g., street tree litter [Hill et al., 2022; Hobbie et al., 2014], fossil fuel combustion [Baker et al., 2001], and fertilizer [Groffman et al., 2004; Hobbie et al., 2017]) as compared with pharmaceuticals, decoupling these two types of contaminants.

Differences in sources between nutrients and pharmaceuticals also lead to differences in the relationship between concentration and discharge as well as likely differences in the export flow distribution of these contaminants. In the urban watersheds of the BES, annual nutrient loads are dominated by fluxes that occur during high flows (Duan et al., 2012; Shields et al., 2008). To our knowledge, there has not been a similar analysis for the export of pharmaceuticals and personal care products, as long-term, high-frequency observations of these contaminants are rare. However, we may speculate that the lack of a clear relationship between the concentration of pharmaceuticals and flow (Figure 4) may mean that relatively frequent stormflows flush pharmaceuticals from groundwater and other storage zones, where they may build up between storms (perhaps as the result of slow leaks from aging infrastructure).

While the concentration of some difficult-to-measure solutes, such as metals and cyanotoxins, can be successfully modeled using machine learning and sensor measurements of water quality (Green et al., 2021; Recknagel et al., 2014), our analysis could not successfully model pharmaceutical concentrations using other water quality parameters. These results suggest that the behavior of pharmaceuticals in urban streams is different from metals and cyanotoxins as well as nutrients, all of which can be successfully modeled using other observations of water quality.

It is common to discuss emerging contaminants and the subset of these described as pharmaceuticals and personal care products together as a group because they tend to share similar origins (manufactured for human use) and regulatory status. However, this categorization elides the very different chemistries, impacts, environmental behaviors, fate, and persistence among different compounds, both within the pharmaceutical and personal care products classification and more broadly across emerging contaminant classes. A similar difficulty has been described with respect to the per- and poly-fluoroalkyl substances (PFAS), emerging contaminants that encompass thousands of distinct chemicals used in various manufacturing processes (Ankley et al., 2021; Guelfo et al., 2021). However, PFAS, by definition, share key chemical characteristics, which is not necessarily true of pharmaceuticals and personal care products. Thus, continuing to study and discuss pharmaceuticals in the environment as a single category of pollutant may obscure differences among compounds and impede our understanding.

Comparing TN and total pharmaceutical concentrations conceptually helps to illustrate why treating pharmaceuticals together as a single class may be problematic. When N species are transformed by biogeochemical processes (e.g., mineralization of organic N, nitrification), the N remains a part of the TN pool we measure (except for gaseous products). In contrast, changes to the organic molecules of pharmaceutical compounds that occur during biotic and abiotic degradation make these undetectable by our methods. Metabolites of pharmaceuticals, even those that are biologically active, are invisible to our analysis and are removed from the "total pharmaceutical" pool. Continued advances in nontarget analysis of organic pollutants (Paszkiewicz et al., 2022; Ruff et al., 2015; Singer et al., 2016) will help to expand the number of compounds and their metabolites that can be monitored. Still, recognizing differences in the impacts and persistence of different pharmaceuticals and their metabolites in future analyses will be important for predicting their quantities and behaviors in the environment.

While complex mixtures of pharmaceutical compounds with varying chemistries, solubilities, and labilities in the environment complicate our ability to predict total pharmaceutical concentrations, our ability to predict detections of even a single compound (trimethoprim) using commonly monitored water quality parameters is poor. Our RF model for trimethoprim detection at the watershed outlet had an error rate greater than 50%. In contrast, similar models for nitrate and TP had error rates less than 20%. This disparity highlights the differences in controls on, and therefore predictability of, traditional versus emerging contaminants. Nitrate and TP enter urban streams from numerous point and nonpoint sources (Groffman et al., 2004; Paul & Meyer, 2001; Walsh et al., 2005) and the potential sources of pharmaceuticals are fewer (as reviewed by Patel et al., 2019). Unlike treated wastewater effluent, leaks or failures in sewage infrastructure are highly temporally variable and highly localized. Furthermore, the specific identities of pharmaceutical compounds released to the environment depend on the pharmaceuticals taken by the population whose sewage drains to that particular leak at that particular time. Put simply, we all excrete nitrogen and

phosphorus, but we each excrete a unique mixture of pharmaceuticals.

Though the drivers of nutrient concentrations in urban streams can be complex and their relative importance can be watershed-specific, they can still be predicted with a good deal of accuracy. Emerging contaminants like pharmaceuticals have fewer, more localized, and more temporally variable sources to the environment, which obstructs predictions. Targeted monitoring of these contaminants at greater spatial and temporal resolution is a necessary first step to understanding the controls on their concentration, which may lead to more successful prediction of concentrations in the environment.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Code (Fork, 2025) is available from the Environmental Data Initiative Data Portal: https://doi.org/10.6073/pasta/3553d0cc21a9562369fa8b2d359cc04d. Data are available from the Baltimore Ecosystem Study through the Environmental Data Initiative Data Portal: pharmaceutical concentration data (Rosi et al., 2021): https://doi.org/10.6073/pasta/36453abc14ce8d6a33711231fdee9792, and nutrient concentration data (Groffman et al., 2024): https://doi.org/10.6073/pasta/324ae2ae26878c981a158b8ee7c45feb.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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