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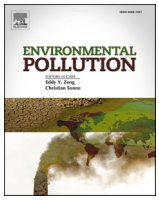

Passive sampler housing and sorbent type determine aquatic micropollutant adsorption and subsequent bioassay responses☆

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ABSTRACT

The combination of integrative passive sampling and bioassays is a promising approach for monitoring the toxicity of polar organic contaminants in aquatic environments. However, the design of integrative passive samplers can affect the accumulation of compounds and therewith the bioassay responses. The present study aimed to determine the effects of sampler housing and sorbent type on the number of chemical features accumulated in polar passive samplers and the subsequent bioassay responses to extracts of these samplers. To this end, four integrative passive sampler configurations, resulting from the combination of polar organic chemical integrative sampler (POCIS) and Speedisk housings with hydrophilic-lipophilic balance and hydrophilic divinylbenzene sorbents, were simultaneously exposed at reference and contaminated surface water locations. The passive sampler extracts were subjected to chemical non-target screening and a battery of five bioassays. Extracts from POCIS contained a higher number of chemical features and caused higher bioassay responses in 91% of cases, while the two sorbents accumulated similar numbers of features and caused equally frequent but different bioassay responses. Hence, the passive sampler design critically affected the number of accumulated polar organic contaminants as well as their toxicity, highlighting the importance of passive sampler design for effect-based water quality assessment.

1. Introduction

Aquatic ecosystems are under threat from an ever-increasing diversity of contaminants that are released into the environment (Bernhardt et al., 2017; Vörösmarty et al., 2010). These contaminants of emerging concern (CECs) are generally (highly) polar and mobile in water, challenging water treatment as well as monitoring technologies (Altenburger et al., 2019; Arp and Hale, 2022; Petrie et al., 2015; Reemtsma et al., 2016). Therefore, there is a need for monitoring methods that enable the sampling, chemical characterization, and toxicity assessment of polar CECs in the aquatic environment. However, conventional toxicity assessment of CECs on an analyte-by-analyte basis is problematic since i) many of the compounds are unknown, ii) if known, toxicity data for these new compounds are very scarce, and iii) mixture toxicity data are even less available. To overcome the drawbacks of traditional water quality monitoring frameworks that are based on a limited number of target pollutants, effect-based methods can be applied to identify the ecotoxicological risks associated with mixtures of (un)known CECs present in the water (Neale et al., 2023). Therefore, bioassay batteries are increasingly applied in water quality assessment, representing a wide range of toxicity endpoints relevant to aquatic ecosystem health (Brack et al., 2019). This allows the ranking of sites

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based on ecotoxicological risks rather than on the presence and absence of contaminants (De Baat et al., 2020, 2019; Hamers et al., 2018; Neale et al., 2015; van der Oost et al., 2017). However, sampling moments and methods critically affect the responses observed in bioassay batteries (Abbas et al., 2019). Since the environmental concentrations of polar organic micropollutants typically vary over time and are, by definition, very low (ng to μg L^{-1}) (Abbas et al., 2019; Roll and Halden, 2016), traditional discrete grab sampling methods provide only snapshots in time of contaminant concentrations and require additional sample enrichment of large water volumes to detect trace level pollutants (Vrana et al., 2005). Passive sampling can overcome these limitations of grab sampling by providing a time-integrative representation of contaminant concentrations in the water while simultaneously allowing the *in situ* pre-concentration of compounds from the surface water (Roll and Halden, 2016; Vrana et al., 2005). The advantages of passive sampling – a time-integrative representation of contaminant concentrations – and bioassays – the identification of the ecotoxicological risks associated with mixtures of all (un)known chemicals – over conventional methods make their combination especially appropriate for the toxicity assessment of the wide variety of (polar) organic chemicals that are present at low and fluctuating concentrations in surface waters.

Integrative (kinetic) passive samplers, here defined as a sampler body that houses a sorbent serving as the receiving phase in which the sampled compounds accumulate, are increasingly used to provide time-integrated measurements of polar organic contaminants in surface waters (Roll and Halden, 2016). The accumulation of polar compounds into integrative passive samplers is governed by the diffusion of the freely dissolved analytes from the surface water across three spatial stages that are inherent to the use of adsorption-based passive samplers in surface water (Harman et al., 2012). The first stage is a viscous layer of water at the surface of the sampler, the so-called water boundary layer (WBL), also referred to as the aquatic or diffusive boundary layer. The second stage is the (membrane) filter used to limit the speed of diffusion of compounds into the sampler and to keep the receiving sorbent phase in place. The final stage is the sorbent itself, to which the analytes ultimately adsorb. The sampler design affects the hydrodynamic conditions in and around the sampler housing, determining the uptake of chemicals into integrative passive samplers (Endo et al., 2019). The sorbent that is applied determines which polar organic compounds can be retained throughout the exposure to the environment (Bäuerlein et al., 2012). These sampler characteristics determine the accumulation of compounds in passive samplers and, in turn, dictate bioassay responses to the passive sampler extracts (Abbas et al., 2019). The choice of the sampler can thus critically affect the outcome of effect-based water quality assessments.

The most widely used type of integrative passive sampler targeting polar compounds in water is the polar organic chemical integrative sampler (POCIS) (Alvarez et al., 2004; Harman et al., 2012), but a variety of alternative devices is available and new sampler configurations are frequently developed. More recently, the commercially available Speedisk® solid-phase extraction (SPE) columns were proposed as a promising passive sampling device (Huysman et al., 2019). Speedisks contain the polymeric sorbent hydrophilic divinylbenzene (H-DVB), which was suggested as a favorable alternative to the commonly used hydrophilic-lipophilic balance (HLB) sorbent for the sorption of organic CECs in passive samplers (Huysman et al., 2019). The robust plastic housing of the Speedisks makes them resistant to damage during field deployment and readily applicable as passive samplers in surface waters. This raises the question of whether this alternative sampler housing and sorbent may be more fit than the well-established POCIS for monitoring polar organic chemicals in aquatic environments. Although separate comparisons of sampler designs (Ahrens et al., 2015; Nguyen et al., 2021) and sorbents (Bäuerlein et al., 2012) on the uptake of polar organic compounds in passive samplers are available, a full-factorial study that allows the simultaneous comparison of multiple sampler housings and sorbents in field-exposed integrative passive samplers has, until now, not been performed. The present study aimed to determine the effects of sampler housing and sorbent type on the number of chemical features accumulated in the polar passive samplers and the subsequent bioassay responses to extracts of these samplers. To this end, four integrative passive sampler configurations, resulting from the combination of the POCIS and Speedisk housings with the HLB and H-DVB sorbents, were simultaneously exposed at reference and contaminated surface water locations. To determine the number of polar organic contaminants accumulated in the passive samplers, a chemical non-target screening was performed on the passive sampler extracts. To measure the toxicity of the accumulated polar organic contaminants, a battery of bioassays for inhibition of bacterial respiration, cytotoxicity, and three reporter-gene bioassays for endocrine disruption was exposed to the sampler extracts. This allowed linking the number of (un)known chemical features to the intensity of the bioassay responses. The outcomes of this study provide insight into the influence of sampler design on compound adsorption and toxicity detection of aquatic organic chemical mixtures, thereby supporting choices of passive sampler characteristics for the application in effect-based surface water quality assessment.

2. Material & methods

2.1. Sampler and sorbent types

The four types of passive samplers used in the present study resulted from the combinations of two types of sampler housing, POCIS and Speedisk (Fig. 1), and two types of sorbent, HLB and H-DVB. The POCIS consists of two stainless steel rings, with an inner diameter of 5.4 cm, that retain the sorbent between two membranes, leaving approximately 46 cm^2 of surface area exposed to the surrounding water (Fig. 1). Speedisks were originally designed as SPE columns, which can be modified to render them suitable for deployment as passive samplers. The Speedisk consists of a plastic housing retaining a sorbent between two glass fiber filters by two plastic screens and a retaining ring (Fig. 1). The bottom side of the Speedisk is sealed, allowing exchange with the surrounding water from only one side of the sampler with an inner diameter of 5.1 cm, leaving an exposure area of approximately 20 cm^2. In the original POCIS design, the receiving phase consists of 200 mg of HLB sorbent (Oasis, Waters, MA, USA), while the original Speedisk contains 400 mg of H-DVB sorbent (Bakerbond, Avantor, Deventer, The Netherlands). The two sorbents were applied in the two sampler housings resulting in four sampler types.

2.2. Sampler preparation

The sorbents were conditioned by eluting with a sequence of organic solvents (Biosolve, The Netherlands; all chromatography grade) and dried under vacuum. For POCIS this was done before sampler assembly using acetone, dichloromethane, and methanol (Supplementary Material S1). For Speedisk this was done after the preparation of the samplers (see below).

For the construction of the POCIS, stainless steel rings (Exposmeter, Sweden), nuts, and bolts, as well as all used tools were cleaned in acetone before the assembly of the samplers. Polyethersulfone (PES) diffusion limiting membrane filters (Pall Corporation, NY, USA; 0.1 μm pore size, 90 mm diameter) were used to enclose 200 mg of either HLB or H-DVB sorbent. The PES membranes were cleaned before the assembly of the POCIS in LC grade methanol:ultra-pure water (50:50, v:v) followed by rinsing in ultra-pure water. After the final assembly, the POCIS were stored at 4 °C in food-grade Mylar zip lock bags until deployment.

For the modification of the Speedisks, the upper half of the Speedisk housings were trimmed to limit the formation of a WBL between the sampler and the surrounding water and to improve the exchange of compounds between the water and the sorbent. Four holes were made in

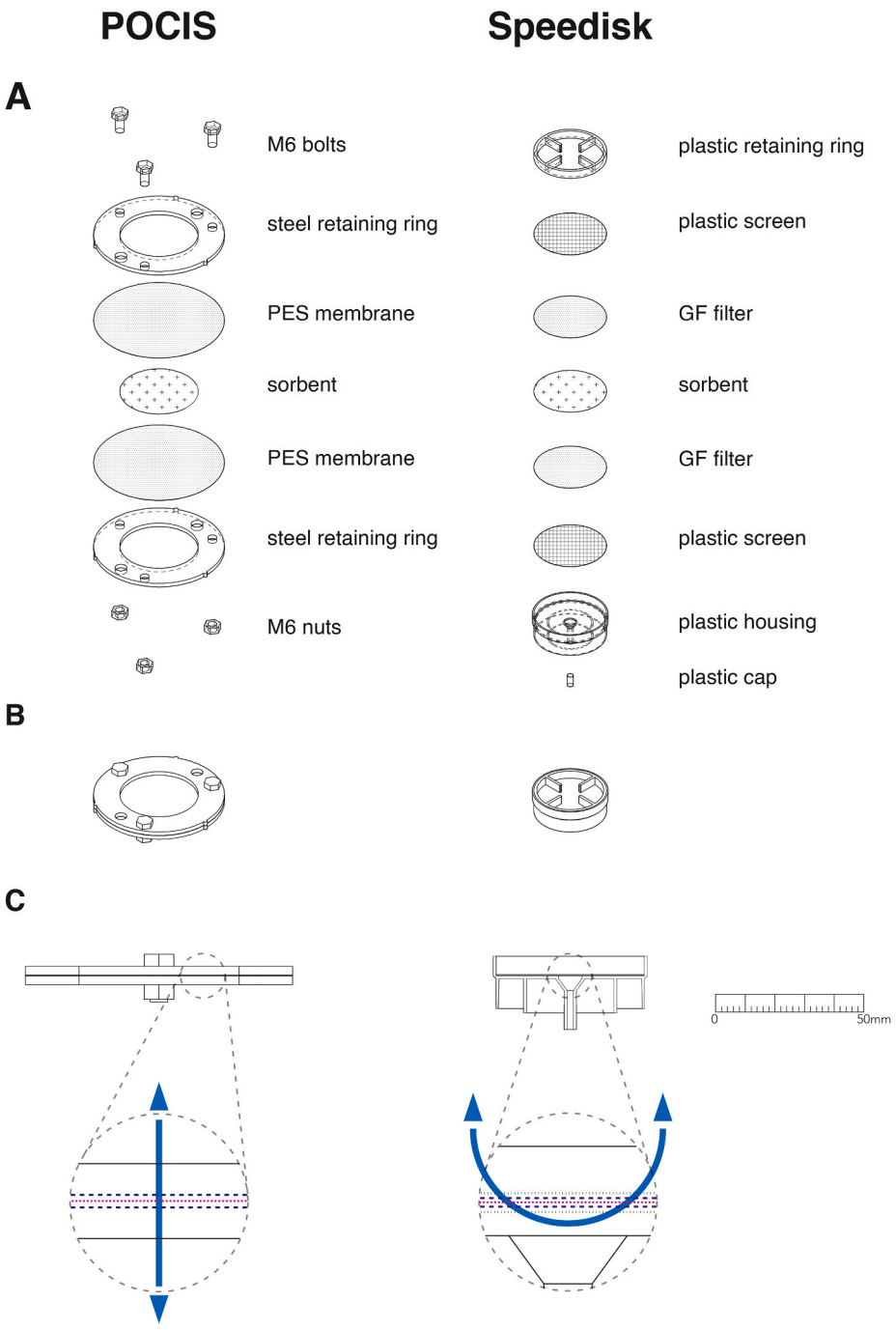

Fig. 1. Technical drawing of polar organic chemical integrative sampler (POCIS) and Speedisk integrative passive sampling devices depicting A: a disassembled 3D view listing the separate passive sampler components (PES = polyethersulfone, GF = glass fiber), B: the 3D assembled configurations, and C: sections with expanded detailed hydrodynamic flow diagrams (dark blue dashed lines represent the membranes/filters, magenta dotted lines represent the sorbent, blue arrows illustrate the water movement through the passive samplers). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

the sorbent-free bottom part of the housing to allow the attachment of the samplers during field deployment. Original Speedisks were advertised to contain 600 mg of H-DVB sorbent. However, upon disassembly, Speedisks appeared to contain only 400 mg of H-DVB sorbent per column, suggesting a discrepancy between the technical details reported by the manufacturer and the final product. Nonetheless, to assess the performance of the HLB sorbent in the Speedisks, these were disassembled and the original sorbent was replaced with 600 mg of HLB, followed by reassembly. All Speedisks were sequentially eluted with dichloromethane, acetone, and ultrapure water (Supplementary Material S1) over a vacuum manifold and the bottoms of the columns were closed with syringe caps to ensure that compound accumulation in the Speedisks during field deployment occurred only by diffusion from the top of the sampler (Fig. 1). The Speedisks were then placed in a jar filled with ultrapure water and stored at 4 °C until deployment.

The amounts of sorbent in both POCIS and Speedisk configurations were previously shown to ensure a linear compound uptake for a wide range of chemicals exceeding the 42 d deployment time used in the present study (Alvarez et al., 2004; de Weert et al., 2020). However, linear uptake for all chemicals that were potentially present cannot be

guaranteed.

2.3. Sampling locations and sampler deployment

Eight lowland streams and drainage ditches in The Netherlands were selected as sampling locations in collaboration with The Dutch regional water authorities. The locations were categorized into three location types (Supplementary Material S2), either surrounded by ornamental flower bulb horticulture (agriculture; n = 3), directly receiving wastewater treatment plant effluent (WWTP; n = 2), or reference locations with no known contamination sources (reference; n = 3). Sampling was conducted between August 20th and October 5th, 2018. The four sampler types were simultaneously deployed for six weeks in quadruplicate at each sampling location, attached to stainless steel cages. To ensure permanent inundation and a continuous flow of water around the samplers while avoiding direct diffusion of compounds from the sediment to the samplers, these cages were attached to stainless steel rods in the middle of the water column. After exposure, biofouling was removed from the samplers using local water and a scrubbing sponge, after which they were transported to the laboratory on ice and stored at −20 °C until extraction.

2.4. Extraction of organic compounds from the passive samplers

The extraction of organic compounds from the passive samplers was performed according to the general protocol described below. The POCIS extractions were performed at the laboratory of the University of Amsterdam (The Netherlands) and Speedisk extractions at the laboratory of TNO (Utrecht, The Netherlands). Slight differences in the extraction procedures due to sampler type-specific characteristics and differences in laboratory equipment are outlined in Supplementary Material (S1). The frozen samplers were freeze-dried overnight. This was done to avoid the loss of more polar compounds when transferring the wet sorbent into the SPE columns using ultrapure water, as is common practice for POCIS. All glassware used in the subsequent extraction procedure was cleaned and dried. After disassembly of the samplers, a glass funnel was used to pool the dry sorbents of the quadruplicates per sampler type per location into an empty 6 mL glass Supelco SPE column with Teflon frit (Sigma-Aldrich, The Netherlands). The sorbent recovery per location was recorded using an analytical balance. The SPE columns were eluted with LC-grade acetonitrile under vacuum on an SPE manifold. The LC-grade acetonitrile that was used in all extractions in both laboratories originated from the same bottle to rule out any confounding influence of the batch of solvent used. A final extract volume of exactly 10 mL was achieved by topping up with acetonitrile by weight after which extracts were stored at −20 °C until analyses. Blanks for all sampler types were obtained by extracting unexposed dry samplers following the same procedure as their exposed counterparts and were included in the subsequent analyses.

2.5. Chemical analysis and non-target screening of passive sampler extracts

Liquid chromatography coupled with high-resolution mass spectrometry (LC-HRMS) was applied to characterize the chemical mixtures accumulated in the different samplers and sorbents. Extracts of each sampler type (POCIS HLB, POCIS H-DVB, Speedisk HLB, and Speedisk H-DVB) for one representative location of each type (agriculture [ag1], WWTP [WWTP1], and reference [ref 2]), as well as unexposed sampler blanks, were selected, resulting in 16 samples. The analyses of the reference standards and the 16 sampler extracts were conducted with a UHPLC system (Nexera, Shimadzu, Den Bosch, The Netherlands) coupled to a Bruker Daltonics maXis 4G high-resolution q-ToF/MS upgraded with HD collision cell and equipped with an electrospray ionization (ESI) source (Bruker, Leiderdorp, the Netherlands). Before UHPLC-q-ToF/MS analysis, the extracts were diluted 5 times in ultrapure water to be more compatible with the aqueous mobile phase used for chromatographic separation. The instrumental methods and reference standards were based on (Narain-Ford et al., 2022). Each sample (20 μL, n = 2) was chromatographically separated with a core-shell Kinetex biphenyl column (100 × 2.1 mm, 2.6 μm particle size, and 100 Å pore size, Phenomenex, Utrecht, the Netherlands) and subjected to HRMS detection in both positive and negative mode. The raw HRMS data were processed with the R programming language (R core team, 2022) using patRoon version 1.2 (Helmus, 2020; Helmus et al., 2021), an open-source platform for comprehensive non-target analysis workflows. The workflow consisted of (1) re-calibration of *m/z* data and export to mzML (Martens et al., 2011) *via* Bruker DataAnalysis, (2) automatic feature extraction and grouping/alignment across samples *via* OpenMS (Röst et al., 2016), and (3) post-treatment of features, by removing features that (3a) have low intensity (<10000), (3b) are present in blanks (unless intensity is 5 times higher), (3c) not present in duplicates or with high-intensity deviation (relative standard deviation > 75%) and (3d) elute before the estimated LC system dead volume (1.5 min, typically originating from the internal mass calibration solution). Features were grouped based on the sampling location, sampler housing, and sorbent type, to visualize unique and common features.

2.6. Toxicity of the passive sampler extracts

The toxicity of the passive sampler extracts was assessed with a battery of five bioassays that were previously shown to be responsive to polar passive sampler extracts (De Baat et al., 2019): i.e. a bacterial bioluminescence inhibition bioassay and *in vitro* chemical activated luciferase expression (CALUX®) bioassays for estrogenic (ERα), *anti*-androgenic (*anti*-AR) and *anti*-progestogenic (*anti*-PR) activities, and cytotoxicity. Results from the latter test were also used to rule out confounding influences of cytotoxicity by the passive sampler extracts on test outcomes of the other three CALUX assays. A 1 mL aliquot of each sampler extract was used for the bacterial bioluminescence inhibition assay and a 2 mL aliquot for the four CALUX assays. Before application in the bioassays, these aliquots were transferred to dimethyl sulfoxide (DMSO). For this, the acetonitrile extracts were dried under constant N_2 flow at room temperature and redissolved in DMSO. Bioassays with the extracts of the four passive sampler types were performed at a 0.1–1% DMSO concentration to improve the compound solubility in the exposure media, always including a control to confirm the non-toxicity of the solvent.

A miniaturized setup of the Microtox® assay, further referred to as the 'bacterial bioluminescence assay', was applied to measure bacterial bioluminescence inhibition using the marine bacterium *Aliivibrio fischeri*, according to Hamers et al. (2001). The bacteria were exposed to dilution series of the passive sampler extracts and luminescence inhibition was measured after 15 min. The *in vitro* cytotoxicity, ERα, *anti*-AR, and *anti*-PR CALUX bioassays were performed according to previously described protocols (Alygizakis et al., 2019) at the BioDetection Systems laboratory (Amsterdam, The Netherlands).

2.7. Data analyses

Toxicity in the bacterial bioluminescence assay was expressed as toxic units (TU), wherein one TU represented the dilution at which the extracts caused a 50% inhibition of bioluminescence (EC_{50}). EC_{50} values were determined by nonlinear regression analysis with the built-in log-logistic model in GraphPad Prism® (GraphPad Software Inc., v. 5.00, San Diego, CA, USA). Responses in the *in vitro* CALUX assays were expressed as bioanalytical equivalent (BEQ) concentrations of the reference compounds. Responses in the ERα assay were expressed as ng 17β-estradiol eq. per mL extract (ng EEQ mL^{-1}), in the *anti*-AR assay as μg flutamide eq. per mL extract (μg FEQ mL^{-1}), in the *anti*-PR assay as ng RU486 eq. per mL extract (ng REQ mL^{-1}), and cytotoxicity as μg tributyltin eq. per mL extract (μg TEQ mL^{-1}). Bioanalytical responses were

corrected for the recovered fraction of the sorbent to account for sorbent loss during the extraction procedure and normalized for the exposure area of the samplers (POCIS 46 cm^2; and Speedisk 20 cm^2). The normalized responses were then compared between the two types of sampler housing and the two types of sorbent. In this comparison, responses were considered higher if they exceeded those from the alternative housing or sorbent, respectively, by >20%. Responses were also considered higher if the alternative housing or sorbent caused no response at all in the bioassays.

3. Results and discussion

3.1. Quality assurance and control

The passive samplers were successfully retrieved from the field and extracted in the laboratory, except for two of the four POCIS H-DVB samplers at location 'WWTP 1', of which the PES membranes were damaged during deployment and which were therefore not included in the subsequent analyses. The five bioassays were successfully performed with all extracts and all assays met their respective validity criteria (Alygizakis et al., 2019; Hamers et al., 2018). Responses in the bacterial bioluminescence inhibition assay were corrected for responses to the blank extracts, while no responses to the blank extracts were observed in the CALUX assays. Dose-response curves for the bacterial bioluminescence inhibition assay are available in Fig. S3 of the Supplementary Material.

3.2. Number of chemical features in passive sampler extracts

The non-target screening revealed that the passive sampler extracts from the WWTP effluent contained substantially higher numbers of chemical features than the extracts from the agricultural site and especially from the reference site, both in positive and negative ionization mode (Fig. 2A). Nonetheless, even in the extracts from the reference sites a substantial number of features was detected (530; positive and negative ionization modes combined). Moreover, the location types had relatively few features in common, emphasizing the presence of many contamination source-specific compounds. When evaluated per sampler housing type, the POCIS sampler extracts contained two to three times more unique features than the Speedisk extracts, but they also had a high number of compounds in common (Fig. 2B). In contrast to sampler housing, the type of sorbent had only a minor influence on the number of identified features (Fig. 2C). Moreover, there were relatively few unique features and the sorbents had most features in common.

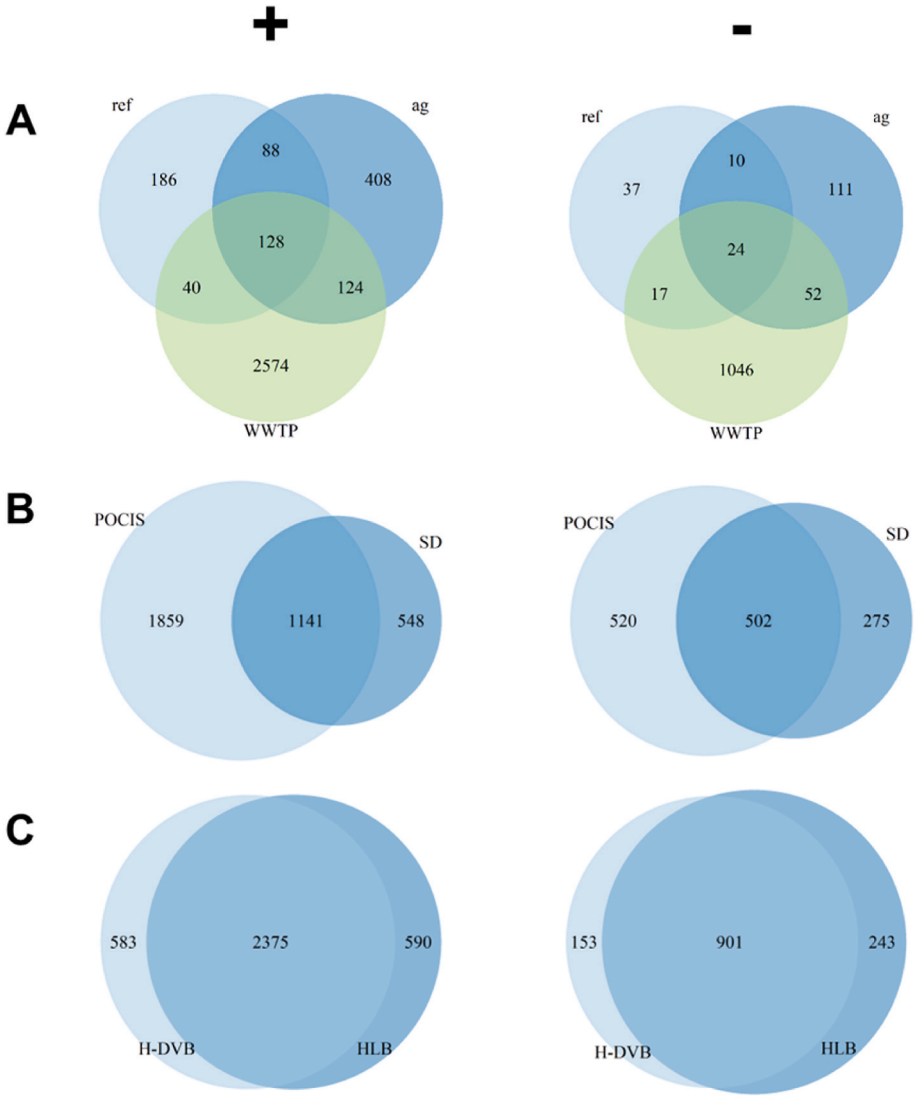

Fig. 2. Numbers of features detected in the non-target screening of passive sampler extracts from three locations in positive (+) and negative (−) ionization mode per A: location type, B: sampler housing, and C: sorbent type. ref = reference, ag = agriculture, WWTP = wastewater treatment plant.

3.3. The influence of sampler housing on the number of chemical features in the passive sampler extracts

Almost twice as many chemical features were detected in the POCIS extracts (4022) compared to Speedisk extracts (2466) (Fig. 2B). The higher number of chemical features detected in the POCIS extracts cannot be attributed to differences in the used sorbents since both types of sorbent were applied in both sampler housings. Hence, the differences in the number of chemical features between POCIS and Speedisk are attributable to differences in the sampler housing. Most notably, these are the size of the sampler exposure area, the thickness of the WBL, and the diffusion across the (membrane) filter. The larger exposed sampler surface area for POCIS (46 cm^2) versus Speedisk (20 cm^2) likely resulted in higher sampling rates, which can cause higher accumulated masses of chemicals in POCIS. This may have resulted in some chemicals being present above the chemical-analytical detection limit in POCIS extracts while still below the detection limit in Speedisk extracts, potentially leading to a lower number of detected features in Speedisk extracts. Since non-target HRMS is not quantitative, a correction of chemical concentrations for the sampler surface area and an evaluation of the influence of surface area on the number of chemical features was not possible. However, this was possible for the bioassay responses, providing more quantitative insights into the differences in chemical accumulation for the different passive sampler housings, which are discussed below. The thickness of the WBL is partly dictated by fluid velocity (Harman et al., 2012), which was identical for all sampler types since they were simultaneously exposed at the same locations. For the other part, the WBL thickness depends on hydrodynamic conditions in the vicinity of the membrane, which are significantly affected by the sampler housing geometry. The depth of the sampler body, i.e. the distance between the outer housing and the surface of the filter, influences the rate of the boundary layer transport of analytes to the filter, where a deeper sampler body effectively reduces passive sampling rates (Lobpreis et al., 2008). The shallower depth of the POCIS (3 mm) compared to the Speedisk (6 mm) may thus very well have resulted in higher sampling rates for POCIS. Similar to sampler depth, obstructions to water movement in the sampler housing can also negatively affect sampling rates. Where the POCIS membrane is in direct contact with the WBL, the Speedisk filter and sorbent are held in place by a plastic screen and a retaining ring (Fig. 1). These physical obstructions are also expected to decrease the convective transport of analytes to the Speedisk filter, further limiting Speedisk sampling rates. These observations suggest that the hydrodynamic conditions in the sampler housings appear to be more favorable for the diffusion of compounds into the POCIS and may thus, at least partly, explain the higher number of chemical features analyzed in the POCIS extracts.

Once compounds have reached the (membrane) filter of the sampler, permeation through the filter can occur either through the water-filled pores or via the filter material itself (Alvarez et al., 2004; Harman et al., 2012). Filters are applied in passive samplers to retain and protect the sorbent, but also to regulate the uptake rate of compounds (Endo and Matsuura, 2018). Hence, the filters intentionally limit the diffusion of compounds to the sorbent to extend the linear uptake phase of compounds into the sampler. Polymeric filters like the PES membranes used in the current study have been shown to substantially limit the uptake rates of compounds in passive samplers, especially for compounds with a log $K_{OW} > 2$ (Endo and Matsuura, 2018; Vermeirssen et al., 2012). This is attributable to the accumulation of hydrophobic compounds in the PES membrane, which leads to a lag in the transfer of these compounds to the sorbent (Vermeirssen et al., 2012). The undesirable sorption of compounds to the filters can be avoided by the use of alternative inert membrane materials, like PTFE (Endo and Matsuura, 2018). The glass fiber filters used in the Speedisks are also expected to exhibit a very low affinity towards compounds and should thus result in faster transport of analytes through the filter. This could result in improved sampling rates, especially for hydrophobic chemicals, compared to samplers in which sorptive polymeric filters are used. Nevertheless, it appears that any advantage of the use of glass fiber filters in the Speedisks for the passive sampling of polar compounds from surface waters was offset by the decreased hydrodynamics resulting from the design of the Speedisk housing.

3.4. The influence of sorbent type on the number of chemical features in the passive sampler extracts

In the present study, the two sorbent types accumulated very similar numbers of compounds (Fig. 2C). The efficacy of H-DVB in the sorption of organic CECs from water was elaborately investigated and compared to that of HLB (Huysman et al., 2019). This revealed a higher degree of cross-linkage and functionalization for H-DVB compared to HLB. These findings are in line with the reported higher extraction efficiencies for a range of nonpolar organic CECs of H-DVB compared to HLB in laboratory studies (Huysman et al., 2017; Vanryckeghem et al., 2019). Indeed, this higher degree of polymer functionalization for H-DVB is expected to provide an improved sorption capacity, especially for nonpolar compounds (Huysman et al., 2019). However, the present results illustrate that the higher sorption capacity of H-DVB did not result in a higher number of detected features *per se*, likely due to the present focus on polar organic contaminants. Hence, in contrast to the sampler housing type, the sorbent type did not substantially influence the number of features detected in the passive sampler extracts.

3.5. Bioassay responses to passive sampler extracts

Responses were observed in all bioassays and for all sampler types (Fig. 3). Extracts from reference locations typically caused relatively low bioassay responses, indicating limited, if any, toxicity compared to agricultural and WWTP locations. Agricultural locations were characterized by the highest responses in the *anti*-PR and *anti*-AR CALUX assays, and to a lesser extent by responses in the ERα CALUX assay. The WWTP locations, contrastingly, were characterized by inhibited bacterial bioluminescence and elevated ERα activities.

3.6. The influence of sampler housing and sorbent type on bioassay responses

The comparison of the bioassay responses between the POCIS and Speedisk housings, independent of the applied sorbents, clearly illustrates the substantially higher responses caused by the POCIS extracts in most bioassays for almost all locations (Fig. 3). Indeed, when quantifying the differences in responses (applying a 20% cutoff value) between the sampler housings, POCIS caused higher responses in 91% of extract *x* bioassay combinations (Table 1). This was observed for the bacterial bioluminescence assay but was especially pronounced for the CALUX *in vitro* assays, in which the Speedisk extracts never caused a response higher than the POCIS extracts. Evidently, the POCIS in the majority of cases accumulated higher amounts of compounds that elicit responses in all of the applied bioassays (Table 1). Since the responses were corrected for the exposure area of the samplers, this cannot be attributed to the higher exchange surface area of the POCIS, but rather is a result of the design of the sampler. Apparently, the POCIS housing allows the accumulation of substantially higher amounts of bioactive compounds from the surrounding surface waters than the Speedisk housing does. The comparison of the bioassay responses between the HLB and H-DVB sorbents, independent of the applied housings, elucidated that the two sorbents caused equal bioassay responses in only 26% of cases (Table 1). However, there was not one sorbent that clearly outperformed the other, as extracts from samplers containing HLB caused higher responses in 39% of cases, and extracts from samplers containing H-DVB caused higher responses in 35% of cases (Table 1). Apparently, both sorbents effectively adsorb a partly different suite of bioactive compounds, perhaps both in terms of identity and quantity, leading to differences in

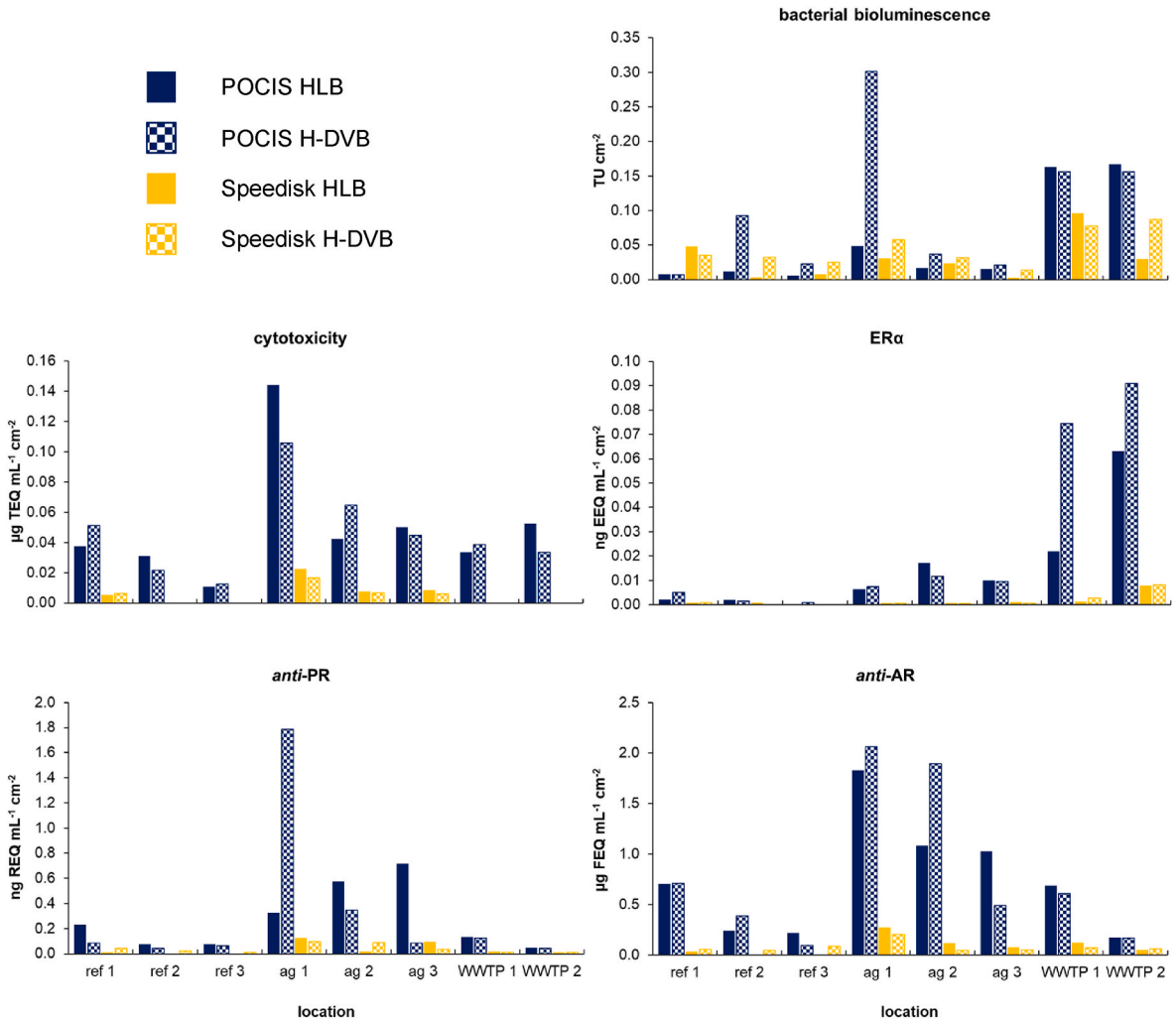

Fig. 3. Bioanalytical responses to extracts from four passive sampler configurations with different housings (POCIS vs. Speedisk) and sorbents (HLB vs. H-DVB) for the bacterial bioluminescence inhibition assay and four CALUX bioassays. Responses were normalized for sampler exposure area and sorbent recovery after extraction. TU = toxic unit, EEQ = 17β-estradiol eq., TEQ = tributyltin eq., REQ = Ru486 eq., FEQ = flutamide eq., ref = reference, ag = agriculture, WWTP = wastewater treatment plant.

Table 1
Comparison of the number of chemical features and the bioanalytical responses to extracts from four types of passive samplers with different housings (POCIS vs. Speedisk) and sorbents (HLB vs. H-DVB). Bioanalytical responses were considered higher (+) when they exceeded responses to extracts from the alternative housing or sorbent, respectively, by >20%.

number of chemical features		bioassay response	TOTAL	%
housing		**housing**		
		equal	3	**4**
POCIS	4022	POCIS +	73	**91**
Speedisk	2466	Speedisk +	4	**5**
sorbent		**sorbent**		
		equal	21	**26**
HLB	4109	HLB +	31	**39**
H-DVB	4012	H-DVB +	28	**35**

POCIS or Speedisk, HLB or H-DVB?.

bioassay responses.

Although many chemicals demonstrate linear uptake in POCIS for periods up to 56 d (Alvarez et al., 2004), a fraction of chemicals may have approached equilibrium in POCIS due to their higher surface area to sorbent mass ratio compared to Speedisk. This would cause uptake curves for some chemicals to start to flatten, leading to somewhat different relative chemical compositions of chemicals in the final extracts (Roll and Halden, 2016). Nonetheless, the samplers were exposed within the duration windows commonly reported in the literature (e.g. de Weert et al., 2020; van der Oost et al., 2017).

The results of the present study revealed that the number of chemical features detected in the passive sampler extracts are in agreement with the bioassay responses to these extracts (Table 1). The POCIS passive samplers accumulated almost twice as many compounds as the Speedisks, and in 91% of cases, the bioassay responses to the POCIS extracts were higher than to the Speedisk extracts. Meanwhile, the sorbent type had little influence on the number of detected features and the overall intensity of the bioassay responses was very similar, albeit with differences in the type of responses (Table 1).

A proposed advantage of the Speedisk is its commercial availability in a robust housing, which simplifies its application as a passive sampler (Huysman et al., 2019). The robustness makes the loss of samplers resulting from damage less likely than with POCIS, in which puncturing or rupturing of the PES membrane sometimes occurs, as was also observed in the present study. Additionally, the Speedisk design as an SPE column can simplify the extraction procedure after deployment. However, biofouling is likely to occur on the surface of passive samplers during extended field deployments. This is an issue if the intact Speedisk

sampler is extracted after field exposure since the co-extraction of compounds accumulated in the biofilm will occur. This is also true for any chemicals that sorb to the plastic housing of the Speedisk during field deployment. To avoid this, the samplers should be disassembled to isolate the sorbent before extraction. The greater robustness of the Speedisk housing alone does not offer a convincing advantage over the use of the POCIS housing, since the Speedisk housing geometry limits the number of detected features, resulting in less frequent and less intense bioassay responses. Following these observations, it is concluded that the use of the POCIS housing results in the better detection of potentially toxic polar organic contaminants in surface waters compared to the Speedisk when using a combination of passive sampling and bioassays. This is in line with a previous study, which found POCIS superior to Speedisk as a passive sampler for effect-based water quality monitoring (Nguyen et al., 2021).

While passive sampler housing influenced both the frequency and intensity of bioassay responses, the choice of sorbent hardly influenced the overall intensity but did affect the type of bioassay responses. Hence, both the sampler housing and sorbent type can determine the outcome of surface water quality assessment strategies by determining which contaminants are available for subsequent analyses. Therefore, a sampler, or a combination of multiple types of samplers, should ideally accumulate all potentially toxic substances from the water so that false-negative toxicity detections are avoided. In the present study, false negatives may have occurred for location 'ag 1', where only the POCIS H-DVB sampler extract caused relatively high responses in the bacterial bioluminescence assay and the *anti*-PR CALUX assay. At this specific location, the other three sampler types appear to have underestimated the presence of toxic levels of a certain compound or group of compounds that caused a toxic response in these bioassays. An elegant solution to limit false negatives to a minimum is the application of multiphasic sampler configurations that apply multiple sorbents with specific characteristics, which have been developed in particular for POCIS (Harman et al., 2012). In some cases, these configurations can indeed result in improved uptake and recovery for certain classes of compounds (Alvarez et al., 2004). Given the anticipated shift in the characteristics of CECs to more highly mobile polar and ionizable compounds (Arp and Hale, 2022; Escher et al., 2020; Reemtsma et al., 2016), future-proof sampler configurations can be developed that house (mixtures of) novel adsorbents with ion-exchanging or extremely polar properties (Augusto et al., 2013). Nonetheless, both HLB and H-DVB can adsorb a wide range of highly polar to moderately nonpolar organic compounds from aquatic matrices (Huysman et al., 2019), and their use as non-selective sorbents in polar passive samplers in surface waters is justified.

3.7. Perspectives for application in water quality assessment

The capacity of a passive sampler to sequester compounds from the environment will determine how effectively potential ecotoxicological risks can be determined when the extracts are applied in bioassays. The integrative passive sampler that provides extracts with the highest number of chemical features and elicits the most frequent and intense bioassay responses will thus allow for the most sensitive environmental risk assessment. Moreover, the high number of features, sometimes up to several thousand, detected in some of the passive sampler extracts in the present study underlines the advantage of bioassays over target chemical analyses in the detection of environmental contaminants. The conversion of bioassay responses to passive sampler extracts into water concentrations has long been a topic of discussion (Jahnke et al., 2016). However, it was recently shown that the conversion of a bioassay response to integrative passive sampler extracts into time-weighted average bioactivities per liter of water seems justified (de Weert et al., 2020). Accordingly, this approach is commonly applied when combining passive sampling with bioanalysis (De Baat, 2020; Leusch et al., 2024; Sonavane et al., 2018; van der Oost et al., 2017). This supports the translation of bioassay responses to actual contamination levels in the field, paving the way for chemical risk assessment based on the combination of passive sampler extracts with effect-based methods. Hence, improved accuracy of sampled volume estimations for integrative polar passive samplers will strengthen ecotoxicological risk interpretations. Furthermore, improvements to sampler designs can be made to enable the integrative sampling of as wide a range of compounds as possible, which is necessary given the changing nature of anthropogenic chemical use.

4. Conclusions

The present study demonstrated that passive sampling is a promising approach for the monitoring of polar organic micropollutants in surface waters. The sampler configuration determines the efficacy of the passive sampling device for the accumulation and sequestration of compounds, and hence the detection of potentially toxic elements in the environment. A substantial body of literature confirms the superiority of passive sampling approaches over conventional grab sampling and supports the application of passive samplers in chemical and effect-based environmental monitoring. Combining passive sampling, non-target screening, and bioassays allows for the detection of the presence and toxicity of a wide range of polar pollutants. This, in turn, highlights the applicability of this combination of advanced tools in water quality monitoring and their use for targeted mitigation measures to protect aquatic ecosystems from the increasing use of chemicals by society.

CRediT authorship contribution statement

M.L. de Baat: Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Conceptualization. **D.M. Narain-Ford:** Writing – review & editing, Investigation. **J. de Weert:** Writing – review & editing, Methodology, Investigation, Conceptualization. **D. Giesen:** Writing – review & editing, Resources. **H. Beeltje:** Writing – review & editing, Resources. **T. Hamers:** Writing – review & editing, Resources. **R. Helmus:** Writing – review & editing, Investigation, Formal analysis. **P. de Voogt:** Writing – review & editing, Supervision. **M.H.S. Kraak:** Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envpol.2024.124488.

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