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Temporal trends of lipophilic organic contaminants in blue mussel (1994–2017) and eelpout (1994–2017) from the southern Baltic Sea

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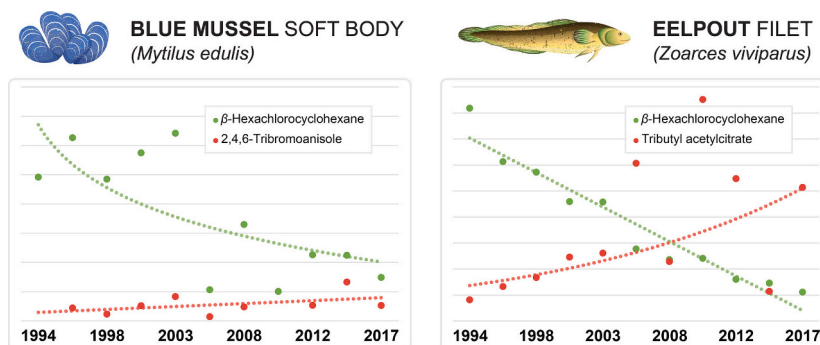
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HIGHLIGHTS

- Time-trend guided non-target screening of Baltic Sea mussel and eelpout using GC-HRMS
- Fast and adjustable data processing workflow for both EI and ECNI data
- >250 tentatively identified organic contaminants showed significant temporal trends
- Four emerging contaminants were reported for the first time in marine biota

GRAPHICAL ABSTRACT



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ABSTRACT

A time-trend study was carried out for two important Baltic Sea species, blue mussel (1994–2017, 11 samples) and eelpout (1994–2017, 11 samples), to track the changes in levels of regulated persistent organic pollutants (POPs) and show potential increases in the levels of the contaminants of emerging concern (CECs). It was carried out utilizing gas chromatography–high-resolution mass spectrometry (GC-HRMS) based non-target screening (NTS). Data were acquired in two modes – electron ionization (EI) and electron capture negative ion chemical ionization (ECNI) – to widen the contaminant coverage, and treated using a fast semi-automated NTS data processing workflow. The study revealed that >250 tentatively identified compounds show statistically significant temporal trends in Baltic blue mussel and eelpout. A large number of regulated substances, including but not limited to PCBs, DDTs and other organochlorine pesticides (OCPs), chlorobenzenes, and many polybrominated diphenyl ethers (PBDEs), showed significant declining trends, as was expected. Their rates of decline were in good agreement with previously reported data. In contrast, increasing trends were observed for many CECs, some polycyclic aromatic compounds (PAHs), and hydrocarbons. The CEC group included, among others, four compounds, namely, one personal care product ingredient, 2-ethylhexyl stearate, one brominated compound 1,2,3,5-tetrabromobenzene and two intermediates 4-isopropoxyaniline and bilobol dimethyl ether, that were reported in marine biota for the first time to the best of our knowledge. Several compounds, including four CECs and two unknown brominated compounds, showed levels considerably higher than the common legacy pollutants (CB-153 and BDE-99), which might be taken into consideration for future monitoring and risk

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assessment. In addition, this work revealed the presence of a plethora of organoiodinated compounds that exhibited statistically significant temporal trends in the samples under study, which could be of future interest.

1. Introduction

Since the dawn of the industrial era, new, apparently useful, chemicals have constantly been introduced into people's everyday lives to improve the quality of living by, for instance, providing pest control to achieve better yields of crops, controlling the spread of, and eradicating, disease, and simply creating new materials, such as plastics, to produce things that surround us. According to the latest European Chemicals Agency (ECHA) report, just in the European market alone, >20,000 various registered chemical substances are used in amounts >1 tonne *per annum*, with approximately 10 % of these being used at levels as high as 1,000 tonnes *per annum* or more (ECHA, 2023a). This potentially means a huge discharge of well-known and new chemicals into the environment. These can be potentially harmful to ecosystem health in the terrestrial, freshwater, and marine environment. In response, the European Union have set up a risk assessment framework for chemicals in use to provide for safer chemical markets, better emission control, and extensive environmental monitoring programs. The latter includes an assessment of the chemical status for prioritized substances and identification of management options, where applicable (EC, 2023a; EC, 2023b). Use of such restrictions for substances result in diversification and substitution of the chemical market. In addition, it results in an increasing number of contaminants of emerging concern (CECs), which are substances that may be candidates for regulation, but have so far not been prioritized for it or for monitoring.

Temporal trend analysis (or time-trending) for substances in environmental media can be used to track the effectiveness of chemical management and to screen for CECs as early warning signals for regrettable substitution. Usually, samples from the same species and location but collected over different years are analyzed for specific chemicals. Then, the acquired data are used for statistical temporal trend analysis, which is usually characterized by annual change (AC) values that give yearly increases or decreases in the levels of a certain chemical. In regulatory programs, data are generated for a short list of priority substances in iterative monitoring programs specified in environmental legislation. In contrast, environmental specimen banks (ESBs), that have been established in the second half of the 20th century all over the world, allow for a broader analytical strategy. Samples from the environment are collected, processed, and archived at ultra-low temperatures according to highly standardized protocols in such a way that they can be used at any time to retrospectively investigate chemicals that were not known to be hazardous in the past, were not detectable using earlier instrumentation, or were simply ignored by chemical management (Koschorreck et al., 2015). In recent decades, ESB samples have been used for retrospective analysis of target analytes to establish spatial and temporal trends of legacy chlorinated, brominated, and fluorinated compounds, their presumed substitutes, and certain CECs. For example, Nyberg et al. (Nyberg et al., 2015) reported AC values for POPs such as polychlorinated biphenyls (PCBs), dichlorodiphenyltrichloroethane (DDT) and its metabolites (known under a collective name of DDTs), hexachlorocyclohexanes (HCHs), and hexachlorobenzene (HCB) in Baltic guillemot, herring, cod, perch, eelpout, and blue mussel, whereas Fliedner et al. (Fliedner et al., 2020) reported temporal trends for several CECs, including flame retardants Dechlorane 602, Dechlorane 603, and Dechlorane Plus, in Baltic eelpout and blue mussel. Samples of the two latter species were analyzed in the current work. However, in this study, we used a non-target screening (NTS) based approach using gas chromatography–high-resolution mass spectrometry (GC-HRMS) instrumentation, which, being untargeted in its nature, allowed for capturing temporal trends of numerous lipophilic contaminant classes simultaneously. The efficiency of such an approach

has already been demonstrated in a similar study on Baltic top consumers (Rebryk et al., 2022).

In the current study, we focus on the base of the Baltic Sea food web and present temporal trend data for >250 tentatively identified compounds, including known (legacy POPs, such as PCBs and DDTs) and new and emerging contaminants, in Baltic Sea blue mussel (*Mytilus edulis*) soft body and eelpout (*Zoarces viviparus*) filet, both represented by 11 samples collected from 1994 to 2017.

2. Materials and methods

2.1. Chemicals and reagents

SupraSolv® grade (for gas chromatography) acetone, acetonitrile, dichloromethane (DCM), diethyl ether, *n*-hexane, isooctane, methanol, anhydrous sodium sulfate (Na₂SO₄) for analysis and Florisil® (0.15–0.25 mm) for column chromatography were purchased from Merck KGaA (Darmstadt, Germany); 99.5 % ethanol was purchased from VWR Chemicals (Vienna, Austria). A GPC Calibration Solution containing corn oil, di(2-ethylhexyl)phthalate, pentachlorophenol, perylene, and sulfur as well as a 28 component PCB standard mixture were purchased from AccuStandard (New Haven, CT, USA). The PCB mixture contained CBs 8, 18, 28, 44, 52, 66, 77, 81, 101, 105, 114, 118, 123, 126, 128, 138, 153, 156, 157, 167, 169, 170, 180, 187, 189, 195, 206, and 209 and was used for PCB congener identification. A 22 component Toxaphene standard mixture consisting of Parlars 11, 12, 15, 21, 25, 26, 31, 32, 38, 39, 40, 41, 42, 44, 50, 51, 56, 58, 59, 62, 63, and 69 (Parlar et al., 1995) was purchased from Dr. Ehrenstorfer GmbH (Augsburg, Germany) and used for toxaphene peak assignment. An isotopically labeled PCB standard, ¹³C₁₂-CB-188, was purchased from Cambridge Isotope Laboratories, Inc. (Andover, MA, USA) and used as a volumetric standard. A GC–MS–RTI solution, containing saturated C7–C40 alkane mixture, was purchased from Supelco (Bellefonte, PA, USA) and used for retention index determination.

2.2. Samples

This study focused on the low-level consumer species of the Baltic ecosystem *i.e.* one filter feeder, blue mussel (*Mytilus edulis*), and one fish species, eelpout (*Zoarces viviparus*). Both species are stationary, have high ecological relevance, and have had documented pollutant-related health effects in the past (Schiedek et al., 2006). In addition, blue mussels are consumed by humans, hence, it is important to monitor the levels of chemical contaminants in their flesh. Blue mussels are sampled and analyzed in coastal monitoring under the Water Framework Directive and the Marine Strategy Framework Directive (EC, 2008). Eelpout has been proposed as one of the preferred sentinel species for monitoring the effects of hazardous substances on the health of the marine environment by the Oslo-Paris Regional Convention (OSPAR) (OSPAR, 2007) and the Helsinki Commission (HELCOM) (HELCOM, 2008). The two species are constantly sampled in the frameworks of various national and international contaminant monitoring programs *e.g.* the National Swedish Contaminant Monitoring Programme (blue mussel since 1980 (Odsjö, 1993) and eelpout since 1989 (Hedman et al., 2011)) and the German Environmental Observation System (blue mussel since 1985 (German Environmental Specimen Bank, 2023a) and eelpout since 1994 (German Environmental Specimen Bank, 2023b)). Both species belong to a benthic food web, have a sedentary life style, and live near the coast *i.e.* closer to the contaminant source, which means they can be good indicators of local pollution. They are in a close trophic relationship as eelpout feed on blue mussels.

Samples were collected, prepared, and stored (at $-130\text{ }^{\circ}\text{C}$) by the German Environmental Specimen Bank, which holds permits for Baltic Sea biota sampling and storage granted by the regional National Park Administration (Die Nationalparkverwaltung). Blue mussel and eelpout were sampled from Darßer Ort (Bodden National Park of Western Pomerania) in the southern Baltic Proper. Since several samples were available for each year in the time series, they were pooled to reduce the intra-sample variability. For more sample information, please see Table S1 in the SI.

2.3. Extraction, clean-up, and fractionation

The procedure for sample extraction, clean-up, and fractionation was described in full in our previous work (Rebryk et al., 2022). In short, the samples were ground with anhydrous Na_2SO_4 (1:4; w/w), extracted with *n*-hexane:acetone (1:2.5, v/v) and *n*-hexane:diethyl ether (9:1, v/v) mixtures according to Jensen et al. (1972) (Jensen et al., 1972), and evaporated until only lipids remained. The lipid content was determined gravimetrically and varied between 0.15 % (blue mussel soft body) and 2.9 % (eelpout filet) (Table S1 in the SI). Then, the bulk of lipids was removed using a two-step high-resolution gel permeation chromatography (HR-GPC) clean-up: the samples (0.35 g of lipids or the whole sample in case its weight was $<0.35\text{ g}$) were re-dissolved, injected (900 μL), and eluted isocratically with a DCM:*n*-hexane mixture (1:1; v/v); a contaminant fraction was collected, concentrated, and re-injected for a second clean-up. Samples were further fractionated using a glass column (i.d. 1.0 cm) filled with Florisil® (8.0 g, deactivated with 1.2 % H_2O , w/w) according to Norstrom et al. (1988) (Norstrom et al., 1988). The first three fractions (*n*-hexane, 15 % DCM in *n*-hexane, and 50 % DCM in *n*-hexane) were retained for instrumental analysis, whereas the fourth fraction (8 % methanol in DCM) contained too much matrix material to be analyzed as was. The eluate volumes were reduced to about 5 mL and the solvent was exchanged to isoctane (fractions 1 and 2) or acetonitrile (fraction 3). A volumetric standard ($^{13}\text{C}_{12}$ -CB-188; 3 ng) was added to each fraction to account for variations in the sample volumes and instrument response, and to act as a common reference for normalization of peak areas across the three Florisil® fractions. Afterwards, the volumes were reduced to 0.3 mL and the samples were transferred to GC vials. Method blank samples were run in the same manner in parallel to the biota samples.

2.4. Gas chromatography–high-resolution time-of-flight mass spectrometry

The full data acquisition procedure and instrument settings used are given in the previous study (Rebryk et al., 2022). In brief, an Agilent 7890B GC instrument coupled to an Agilent 7250 QTOF-MS (both Agilent Technologies, Santa Clara, CA, USA) system, operating in electron ionization (EI) or methane electron capture chemical ionization (ECNI) mode, was used. ECNI was used to selectively screen for brominated and iodinated compounds. The injection volume was 1 μL . The system was tuned using perfluorotributylamine (PFTBA). After an initial autotune, the ion source and ion optic settings were manually optimized. Frequent recalibration of the mass scale (once per batch of 10–15 samples) was undertaken: the mass error was $<2\text{ ppm}$. Frequent retention time reproducibility checks were also undertaken. All analyses were carried out in a randomized order. (Linear) retention index ((L)RI) assignment was done using the so-called alkane ladder utilizing a mixture of saturated C7–C40 alkanes.

2.5. Time-trend directed non-target screening workflows

The main focus of the data processing in this work was discovery and further identification of the features that showed statistically significant temporal trends (upward or downward; characterized by annual change (AC) value) in the samples under study. Peak picking, peak area

determination, and spectral library search were carried out using MassHunter 10.0 Suite (Agilent Technologies, Santa Clara, CA, USA). Data alignment, prioritization, and time-trend analysis were carried out using KNIME Analytics Platform (version 4.7.1; KNIME AG, Zurich, Switzerland) and Python 3 scripts (version 3.9.13; Python Software Foundation, Wilmington, DE, USA).

The non-target screening (NTS) workflow for the EI data used here is similar to the one used in our previous time-trend study (Rebryk et al., 2022), whereas the ECNI part of the workflow was adjusted from the previous version, in which manual brominated compound alignment was used, to one based on automated alignment. In addition, iodinated compound screening was added to the ECNI workflow. Finally, since many KNIME nodes were deprecated in the most recent version (4.7.1), all parts of the workflows were adjusted and deprecated nodes were replaced. These fast, adjustable, and highly automated time-trend (TT) directed NTS workflows are hereby referred to as TT-NTS. The full descriptions of the TT-NTS workflows are available in the SI, Workflows S1 and S2.

2.5.1. Time-trend directed non-target screening (TT-NTS) of EI data

A set of custom libraries, containing compounds that are frequently found (detection frequency $>65\%$) in top consumer samples, was developed in our previous study (Rebryk et al., 2022); see sub-section 2.5.1.1. These were re-used in the current study to screen for, and tentatively identify, compounds in lower trophic level samples which increase in concentration over time, eventually leading to increasing exposure of species at higher trophic levels.

The custom libraries include both compounds that could be matched to compounds in the NIST 2020 EI mass spectral library (National Institute of Standards and Technology, Gaithersburg, MD, USA), denoted “hits”, and compounds that did not match, denoted “non-hits”. This approach was used for two reasons: i) to reduce the time needed for library searching (NIST 2020 library contains 350,704 EI spectra (NIST, 2020); the custom “hits” and “non-hits” libraries contain around 3500 compounds in total), and ii) to capture new and emerging compounds, which are sparingly covered by the NIST 2020 library.

The core of the TT-NTS workflow for EI data consists of the following main steps: i) peak picking and deconvolution in MassHunter Unknowns Analysis (UA); ii) NIST 2020 EI mass spectral library search using UA; iii) custom libraries export using MassHunter Library Editor (LE): “hits” libraries contained features matched to the entries in the NIST 2020 library ($\geq 60\%$ spectra similarity) with tentative names assigned, whereas “non-hits” libraries contained unknown (unmatched) features with retention time (RT) identifier assigned; iv) detection frequency filtration: features that are not found in a minimum of two reference samples out of three are removed from the libraries; v) procedural blank filtration (blank : reference sample ratio > 0.2): features abundant in the blank are removed from libraries based on the lipid weight normalized (l.w.) relative response (RR) between the component and volumetric standard ($^{13}\text{C}_{12}$ -CB-188) areas; vi) re-processing of the reference samples using quantitative method in MassHunter TOF Quantitative Analysis (TOFQA) to detect all the features across the reference samples; vii) master custom libraries creation for each Florisil® fraction using UA and LE; viii) sample batch screening in TOFQA using master custom libraries to detect all the features across the samples; ix) time-trend analysis; x) time-trend based filtration; xi) anthropogenic filtration: features whose spectra contain only low-mass fragments (e.g. lipid and petroleum residues) are removed from the list based on specific m/z values, xii) “non-hits” prioritization: 120 features with the highest score are selected for manual structure elucidation using a dot product scoring function (based on detection frequency, maximum abundance (RR l.w. rank), and AC value), and xiii) manual review carried out by structure confirmation/verification by comparison to reference standards or structure confirmation/verification by comparison to mass spectra and RIs from literature, or formula generation and manual structure elucidation, or tentative structure assignment.

2.5.1.1. Custom libraries. In this study, steps i)–vii) of the workflow (section 2.5.1) were missed out as a set of custom libraries had been previously developed based on the screening results of the three Baltic top consumers (harbor porpoise, guillemot, and white-tailed sea eagle from 2017 to 2019) for the three Florisil® fractions. These libraries were already filtered using the aforementioned steps (Rebryk et al., 2022), therefore, they were omitted in this work. The most recent samples of the aforementioned Baltic top consumers were used in that case as they should contain higher amounts of new and emerging contaminants (Rebryk et al., 2022). One of the advantages of using these top consumer-based libraries is the fact they contain a wide range of the contaminants at relatively high levels, as compared to eelpout or blue mussel, and hence, the spectra quality is higher.

Many of the compounds in the custom libraries have been already tentatively identified (Rebryk et al., 2022; Haglund and Rebryk, 2022; Rebryk and Haglund, 2022). However, a large number of features in the custom libraries remain unidentified. These include the features that: i) did not show statistically significant temporal trends or biomagnification in our previous studies, ii) did show significant temporal trends or biomagnification but were not possible to identify using the available information, or iii) did show significant temporal trends or biomagnification but were of limited interest, such as lipids. The full description of the custom library development process as well as the custom library files that include general and spectral information of tentatively identified compounds can be found in the SI, Workflow S1 and Library files S1–S6, respectively.

2.5.1.2. Sample screening for EI features with temporal trends. Three batches of samples, one for each Florisil® fraction, were screened for the features included in the “hits” and “non-hits” master libraries (a total of six) using TOFQA (see Workflow S1.11 in the SI).

Next, TOFQA result tables were exported as Excel files for further time-trend analysis and filtration using KNIME workflows with embedded Python 3 scripts. In brief, the following steps were applied: i) RR l.w. values calculation for each feature using TOFQA feature and volumetric standard (¹³C₁₂-CB-188) peak areas and lipid weight of the respective samples; ii) duplicate removal (originating from different master libraries); iii) sum of RR l.w. calculations for features present in multiple Florisil® fractions; iv) detection frequency filtration (>50 %); v) time-trend analysis using the Mann-Kendall (MK) test; vi) MK *p*-value based cutoff ($p \leq 0.2$; increased from the conventional $p \leq 0.05$ to compensate for peak picking algorithms flaws); vii) annual change (AC, in %) calculation using Theil-Sen regression (TSR); viii) AC value based cutoff ($+1 \% < AC < -1 \%$); ix) anthropogenic filtration; x) “non-hit” features prioritization; xi) manual review. For detailed information see Workflow S1.12–15 in the SI.

2.5.2. Time-trend directed non-target screening (TT-NTS) of ECNI data

Since several important contaminant classes contain bromine (Br), which is easily fragmented in EI mode, a complementary GC–MS acquisition technique – ECNI – was used. In this study, we also included iodine (I) containing compounds, which proved to be abundant in the benthic samples. The halogen ions were targeted and peak lists that contain retention time (RT) information for the Br or I containing compounds were created instead of full-spectrum custom libraries. Hence, the ECNI part of the workflow consists of the following main steps: i) peak picking, smoothing, and integration of combined ⁷⁹Br and ⁸¹Br ions (78.9189 Da and 80.9168 Da, respectively) or ¹²⁶I (126.9045 Da) in the reference samples (the first and last years' samples of each species and all three Florisil® fractions) using MassHunter Qualitative Analysis (QA); ii) peak tables (RT information) export as Excel files using QA for each fraction and species; iii) RT-based alignment of the peak tables entries between the first and last years' samples of each species and the three Florisil® fractions using KNIME to obtain three separate peak lists and to filter out duplicate entries; iv) manual TOFQA method

creation based on the three peak lists (RT information); v) reference sample batch screening in TOFQA; vi) outlier review and TOFQA method refinement; vii) sample batch screening in TOFQA and result tables export as Excel files; viii) noise feature filtration in KNIME (based on peak area) and further TOFQA method refinement; ix) sample batch re-processing using the refined method in TOFQA and result tables export; x) time-trend analysis; xi) time-trend based filtration; xii) manual review (see the next sub-section). See Workflow S2 in the SI for full information.

The time-trend analysis was carried out with the same steps as for the EI data using KNIME and Python 3 scripts (see sub-section 2.5.1.2). For the brominated features that showed significant temporal trends, a manual review was carried out using the following structure elucidation approaches: i) major peak assignment based on comparison to retention indices (RIs) from the previous studies (Rebryk et al., 2022; Rebryk and Haglund, 2022; Rebryk and Haglund, 2021); ii) assignment of additional polybrominated diphenyl ethers (PBDEs), polybrominated biphenyls (PBBs), 1'-methyl-1,2'-bipyrroles (MBPs), and 1,1'-dimethyl-2,2'-bipyrroles (DBPs) using extracted ion chromatograms (EIC) and comparison with literature data (Nordlöf et al., 2010; Stapleton, 2006; Strid et al., 2010; Vetter et al., 2008; Vetter and Rosenfelder, 2008; Wei et al., 2010); iii) generation of potential molecular and fragment formulae and manual structure elucidation.

In the case of iodinated features, the manual review step was missed out as it was impossible to identify the compounds based on the available spectral data. The bond between iodine and carbon is weak and, hence, the molecules dissociate readily – yielding exclusively iodine ions. See the Results and discussion section for suggestions on how this problem can be solved.

3. Results and discussion

3.1. Data processing and time-trend filtration for EI data

From data processing and filtration of the EI “hit” data, 209 features that showed statistically significant temporal trends in archived blue mussel and eelpout samples (collected for a 23-year period) were found. This number corresponds to 7 % of the initial number of features in the “hit” libraries (3,168 entries; see Fig. 1A).

Of the initial 3,168 features (Fig. 1A), almost half were removed in the two custom library refinement steps, namely detection frequency and blank filtration (Rebryk et al., 2022), resulting in 1,625 features (51 %). To be considered for the time-trend analysis, a given feature had to be detected in at least six out of 11 samples for both blue mussel and eelpout. After the MK test-based time-trending, approximately 22 % were removed by *p*-value filtration. Another 2 % were removed after applying the annual change (AC) cutoff ($1 \% < AC < -1 \%$). During anthropogenic filtration *i.e.* removal of biogenic compounds of limited interest, an additional 10 % of the initial number of features were subtracted. The last most rigorous step – manual review – reduced the “hit” list to 209 unique tentatively identified features.

In the EI “non-hit” category, 120 features were short-listed from the total of 540 “non-hits” that showed significant trends (see section 2.5.1). Those were subjected to manual review, which resulted in 22 characterized features at different identification confidence levels (CLs; CL 1 is the highest/the best and means that structure was confirmed using a reference standard, followed by CL 2 (plausible structure), CL 3 (tentative structure), CL 4 (molecular formula), and CL 5 (molecular mass) (Schymanski et al., 2014)). For more information, see Table 1 and Tables S2 and S3 in the SI.

3.2. Data processing and time-trend filtration for ECNI data

The peak picking procedure of features that contain bromine resulted in a total of 1699 features detected in the samples of three Florisil® fractions of both species under study (Fig. 1B). These were further

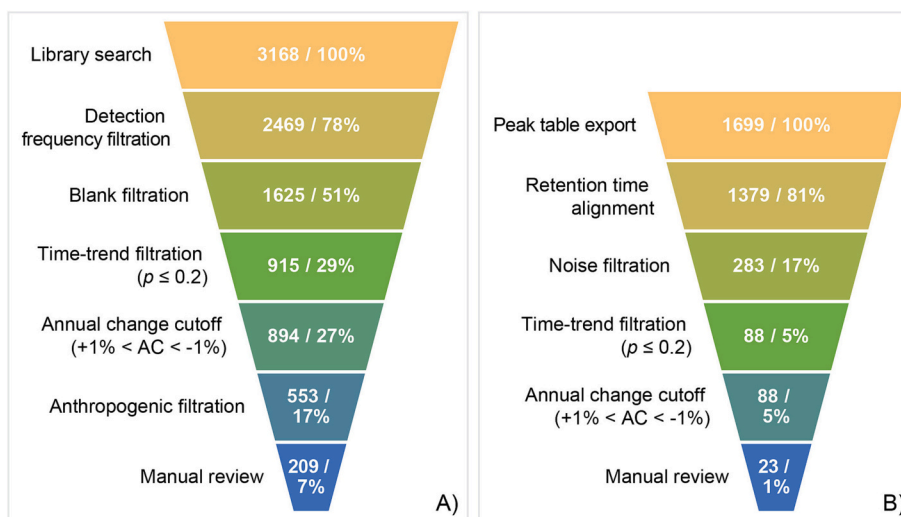


Fig. 1. Total number and percentage of NIST 2020 matched features (“hits”) detected among EI data (A) vs. features detected among ECNI Br data (B) after each filtration step.

filtered based on various steps, slightly different from the ones used for the EI data filtration. First, retention time (RT) alignment was carried out for the first and last year's (1994 and 2017) samples and duplicate features (peaks) were removed. This resulted in removal of approximately 19 % of features. Then, detection frequency filtering (minimum 50 %) and noise filtration (minimum peak area 500) was carried out. This step resulted in removal of approximately 64 % of features. Next, the same two steps as for the EI data were followed, namely, time-trend filtration and annual change cutoff, removing 12 % of features in total. Notably, all 12 % were removed based on the p -value ($p \leq 0.2$) cutoff. Finally, after the manual review and formula elucidation, only 1.4 % of the initial features were left. These 23 features were classified at different CLs (from CL 2 to CL 5), of which nine features were assigned CL 5, as it was only possible to assign Br ions for those. For more information, see Table 1 and Table S4 in the SI.

A similar workflow was used to detect iodine containing compounds. This screening revealed 1,093 features after initial peak table export for both blue mussel and eelpout samples, of which 134 features exhibited significant temporal trends. For more information, see Table S4 in the SI and section 3.4.7.

3.3. Overview of temporal trend data

An overview of the results for EI and ECNI data (excluding iodinated features) is shown in Fig. 2. This shows features with increasing (Fig. 2A) and decreasing (Fig. 2B) temporal trends in the samples of blue mussel and eelpout.

The compounds of main interest for chemical management are found in the “Identified” segments. As can be seen, it was possible to identify 31 features tentatively (28 using EI and 3 using ECNI) that showed increasing trends in blue mussel and 33 features in eelpout samples (29 + 4). As for the features with decreasing trends, 141 features were detected in blue mussel (127 + 14) and 168 features in eelpout samples (162 + 6). The identified compounds are further discussed in the following sub-sections.

The group labeled “Unknown” contains features for which it was impossible to assign a compound name or even formula, as the spectra of those contained only non-specific low m/z ions or generally were of a poor quality. The number of unknown compounds among the EI data exhibiting increasing trends was around one-and-a-half times higher than the number of compounds with decreasing trends (130 (45 + 75) and 88 (62 + 26), respectively) whereas, for ECNI data, the number of brominated compounds with increasing trends was more than double

that of those with decreasing trends (35 (33 + 2) vs. 15 (4 + 11), respectively).

The greatest number of identified compounds with both increasing (33) and decreasing trends (168) was found in eelpout.

3.4. Tentatively identified compounds with statistically significant temporal trends

The results of time-trend analysis are characterized by annual change (AC) values, which show the percentage of yearly increase or decrease in the levels of a particular chemical or compound class over time. An overview of AC values is presented in Fig. 3. The compound classes for the two species are arranged in order of decreasing median class AC values from left to right. In general, most of the compound classes had decreasing (based on median AC values) temporal trends in both species under study.

All tentatively identified compounds with statistically significant temporal trends (254 features in total; see Table 1 and Tables S2 and S3 in the SI) were divided into chemical classes among which legacy POPs, such as DDTs, other organochlorine pesticides (OCPs), and PCBs (84 features accounting for around 33 % of total tentatively identified features), dominated the samples. Many of these were highly abundant, making the detection of the less abundant, but from a regulatory perspective more interesting, CECs challenging, but still possible. Approximately 82 % of the features come from the “hits” sub-part of the EI data processing workflow, whereas the EI “non-hits” sub-part and the ECNI data processing workflow each contributed approximately 9 % of the total number of features.

Additionally, the identified compounds were grouped according to their identification confidence levels and those with the lowest identification confidence levels, namely, with only molecular formulae (CL 4) or exact mass (CL 5) information available, were sorted into separate tables (Tables S3 and S4 in the SI). Also, all the PCBs were moved to SI, Table S2 and only seven indicator PCB congeners were included in Table 1. The identities of 25 compounds (23 PCBs and two toxaphenes (Parlar compounds)) were confirmed at CL 1 using reference standards (see sub-section 2.1). All the tentatively identified compounds are discussed in detail in the following sections.

3.4.1. Contaminants of emerging concern (CECs)

To identify CECs, which are currently not regulated or prioritized for regulatory environmental monitoring was the top priority for this study. Based on the data for both species and using a combination of the three

Table 1

Annual changes (ACs), *p*-values, formulae, CAS#, identification confidence levels (CLs), and linear retention indices (LRIs) for the tentatively identified compounds with significant temporal trends ($p \leq 0.2$) in samples of blue mussel (soft body) and eelpout (filet). In case of co-elutions, formula and CAS# of the main feature are provided.

Class	Feature	Formula	CAS#	CL	LRI	Blue mussel soft body		Eelpout filet	
						AC, %	<i>p</i> -value	AC, %	<i>p</i> -value
Hydrocarbon	3-Hexyl-1-cyclohexene	C12H22	15232-78-7	3	1231	12	0.036	-12	0.016
Hydrocarbon	1-Hexylcyclohexene	C12H22	3964-66-7	3	1241	17	0.016	-18	0.024
Hydrocarbon	(3 <i>E</i>)-3-Tetradecene	C14H28	41446-68-8	3	1386	13	0.128		
Hydrocarbon	1-Pentadecene	C15H30	13360-61-7	3	1480	10	0.025		
Hydrocarbon	(2 <i>Z</i> ,4 <i>E</i>)-3,7,11-Trimethyl-2,4,10-dodecatriene	C15H26	172549-29-0	3	1491			-7	0.060
Hydrocarbon	<i>trans</i> -1-Methyl-2-nonyl-cyclohexane*	C16H32	N/A	3	1586	13	0.186		
Hydrocarbon	(3 <i>E</i>)-3-Heptadecene	C17H34	68155-00-0	3	1682	9	0.060	-6	0.010
Hydrocarbon	Pristane	C19H40	1921-70-6	3	1705	8	0.128	-2	0.073
Hydrocarbon	2-Phytene	C20H40	2437-93-6	3	1828			-2	0.052
Hydrocarbon	Phytadiene	C20H38	N/A	3	1860			-5	0.016
Hydrocarbon	Eicosadiene	C20H38	N/A	3	1878	15	0.177	-7	0.024
Benzene	1,2-Diethyl-3,4-dimethylbenzene	C12H18	28013-18-5	3	1231	-6	0.139		
Benzene	1,2,4-Triethylbenzene	C12H18	877-44-1	3	1239	-4	0.102	-2	0.186
Benzene	1,1'-Diphenylethane	C14H14	612-00-0	2	1524	-5	0.073		
Benzene	(1-Methylnonyl)benzene	C15H22	4537-13-7	2	1596			-2	0.186
Benzene	(1-Pentylhexyl)benzene	C17H28	4537-14-8	2	1625			-4	0.186
Benzene	(1-Butylheptyl)benzene	C17H28	4537-15-9	2	1629			-4	0.139
Benzene	(1-Propylloctyl)benzene	C17H28	4536-86-1	2	1640			-2	0.186
Benzene	(1-Pentylheptyl)benzene	C18H30	2719-62-2	2	1724			-5	0.102
Benzene	(1-Propylonyl)benzene	C18H30	2719-64-4	2	1742			-5	0.102
Benzene	(1-Methylundecyl)benzene	C18H30	2719-61-1	3	1803			-3	0.102
Benzene	(1-Pentylloctyl)benzene	C19H32	4534-49-0	2	1823			-6	0.139
Benzene	1,3-Dimethoxy-5-pentadecylbenzene	C23H40O2	23032-48-6	3	2647	12	0.004		
Benzene	1,3-Dimethoxy-5-hexadecylbenzene*	C24H42O2	N/A	3	2711	5	0.128		
2-ring aromatic	2-Methylnaphthalene	C11H10	91-57-6	3	1295			-11	0.036
2-ring aromatic	1-Methylnaphthalene	C11H10	90-12-0	3	1309			-8	0.073
2-ring aromatic	Biphenyl	C12H10	92-52-4	3	1378			-10	0.024
2-ring aromatic	1,3-Dimethylnaphthalene	C12H12	575-41-7	3	1417			-10	0.036
2-ring aromatic	1,6-Dimethylnaphthalene	C12H12	575-43-9	3	1421			-10	0.024
2-ring aromatic	2-Ethylbiphenyl*	C14H14	1812-51-7	3	1489			7	0.052
2-ring aromatic	2,4'-Dimethylbiphenyl	C14H14	1166-18-3	3	1503			5	0.026
2-ring aromatic	Dibenzofuran	C12H8O	132-64-9	2	1513			-6	0.102
2-ring aromatic	2,2'-Dimethylbiphenyl	C14H14	605-39-0	3	1537	-5	0.024	4	0.186
2-ring aromatic	3,3'-Dimethylbiphenyl	C14H14	612-75-9	3	1587			4	0.024
PAH	Anthracene	C14H10	120-12-7	2	1785	-5	0.036		
PAH	<i>o</i> -Terphenyl	C18H14	84-15-1	3	1877	-8	0.036	-6	0.016
PAH	Methylanthracene/methylphenanthrene	C15H12	N/A	3	1892	-7	0.036	2	0.186
PAH	1-Methylphenanthrene	C15H12	832-69-9	3	1909	-10	0.024	2	0.073
PAH	Fluoranthene	C16H10	206-44-0	3	2051	-10	0.036		
PAH	Pyrene	C16H10	129-00-0	2	2102			-8	0.052
PAH	<i>o,m</i> -Quaterphenyl	C24H18	1165-57-7	3	2595	-5	0.052	-4	0.180
PAH	9,9'-Spirobifluorene	C25H16	159-66-0	2	2656	-3	0.186	-5	0.102
PAH	Benzo[<i>e</i>]pyrene	C20H12	192-97-2	2	2772	-12	0.039		
PAH	Perylene	C20H12	198-55-0	3	2818	-9	0.013		
PAH	<i>m,m</i> -Quaterphenyl	C24H18	1166-18-3	2	2924	-3	0.102		
Cl-benzene	1,2,4,5-Tetrachlorobenzene	C6H2Cl4	95-94-3	3	1323	-6	0.189		
Cl-benzene	1,2,3,4-Tetrachlorobenzene	C6H2Cl4	634-66-2	3	1370			-4	0.016
Cl-benzene	Pentachlorobenzene	C6HCl5	608-93-5	2	1506			-5	0.036
Cl-benzene	Hexachlorobenzene	C10H5Cl7O	118-74-1	2	1689			-3	0.139
Cl-benzene	Octachlorostyrene	C8Cl8	29082-74-4	2	2021			-5	0.016
PCB	CB-28/31	C12H7Cl3	7012-37-5	1	1866	-5	0.036	-6	0.004
PCB	CB-52/43	C12H6Cl4	35693-99-3	1	1934	-4	0.040	-5	0.052
PCB	CB-101/113	C12H5Cl5	37680-73-2	1	2106			-3	0.095
PCB	CB-118	C12H5Cl5	31508-00-6	1	2234	-4	0.139	-5	0.073
PCB	CB-153/132/168	C12H4Cl6	35065-27-1	1	2280	-4	0.139	-5	0.036
PCB	CB-138/158/160	C12H4Cl6	35065-28-2	1	2336	-4	0.102	-5	0.102
PCB	CB-180/193	C12H3Cl7	35065-29-3	1	2484			-6	0.102
PCT	Cl ₂ -terphenyl*	C18H12Cl2	N/A	3	2066	-4	0.138	-4	0.024

(continued on next page)

Table 1 (continued)

Class	Feature	Formula	CAS#	CL	LRI	Blue mussel soft body		Eelpout filet	
						AC, %	p-value	AC, %	p-value
PCT	Cl ₄ -terphenyl	C18H10Cl4	N/A	3	2726	-4	0.177		
PBDE	BDE-49**	C12H6Br4O	243982-82-3	2	2440	-5	0.177	-12	0.073
PBDE	BDE-47	C12H6Br4O	5436-43-1	2	2496	-9	0.010	-11	0.016
PBDE	BDE-100**	C12H5Br5O	189084-64-8	2	2670	-11	0.154	-6	0.095
PBDE	BDE-99**	C12H5Br5O	60348-60-9	2	2736	-8	0.243	-13	0.154
PBDE	BDE-155**	C12H4Br6O	35854-94-5	2	2853			1	0.073
PBDE	BDE-154 (+ co-eluting BB-153)**	C12H4Br6O	207122-15-4	2	2905	-6	0.139		
PBDE	BDE-153**	C12H4Br6O	68631-49-2	2	3001	-4	0.102	-8	0.095
PBDE	BDE-182**	C12H3Br7O	442690-45-1	2	3274	-9	0.006		
DDT	<i>p,p'</i> -DDMU	C14H9Cl3	1022-22-6	2	2097	-6	0.052	-8	0.010
DDT	<i>o,p'</i> -DDE	C14H8Cl4	3424-82-6	2	2097	-7	0.016	-8	0.006
DDT	<i>p,p'</i> -DDE	C14H8Cl4	72-55-9	2	2166	-5	0.052	-6	0.010
DDT	<i>p,p'</i> -DDMS	C14H11Cl3	262-80-0	2	2179	-8	0.016	-9	0.036
DDT	1-(4-Chlorophenyl)-1-(2,4-dichlorophenyl)-2-chloroethylene	C14H8Cl4	18264-62-5	2	2200	-3	0.128	-5	0.016
DDT	<i>p,p'</i> -DDD	C14H10Cl4	72-54-8	2	2254	-8	0.016	-12	0.016
DDT	<i>o,p'</i> -DDMU*	C14H9Cl3	14835-94-0	2	2254			-9	0.016
DDT	<i>p,p'</i> -DDT	C14H9Cl5	50-29-3	2	2335	-8	0.006	-11	0.010
OCP	β -Hexachlorocyclohexane	C6H6Cl6	319-85-7	2	1733	-5	0.139	-8	0.004
OCP	Heptachlor epoxide	C10H5Cl7O	1024-57-3	2	2038	-5	0.060		
OCP	Octachlor epoxide	C10H4Cl8O	27304-13-8	2	2038			-11	0.001
OCP	<i>cis</i> -Chlordane	10H6Cl8	5103-71-9	3	2113	-7	0.025	-8	0.036
OCP	<i>trans</i> -Nonachlor	C10H5Cl9	39765-80-5	3	2120	-4	0.128	-6	0.102
OCP	Dieldrin	C12H8Cl6O	60-57-1	2	2168	-3	0.180		
OCP	Parlar 26	C10H10Cl8	142534-71-2	1	2196			-5	0.016
OCP	<i>cis</i> -Nonachlor	C10H5Cl9	5103-73-1	3	2246	-7	0.128	-6	0.024
OCP	Parlar 40/41	C10H10Cl8	166021-27-8	1	2320			-7	0.036
CEC	4-Isopropoxyaniline	C9H13NO	7664-66-6	3	1316			6	0.102
CEC	2,4,7,9-Tetramethyl-5-decyl-4,7-diol	C14H26O2	126-86-3	3	1405			3	0.139
CEC	2,6-Bis(1,1-dimethylethyl)phenol	C14H22O	128-39-2	2	1430	-6	0.180	5	0.052
CEC	Benzophenone	C13H10O	119-61-9	2	1624	-7	0.139	4	0.036
CEC	1,2,4,5-Tetrabromobenzene**	C6H2Br4	636-28-2	3	1742	-11	0.139		
CEC	1,2,3,5-Tetrabromobenzene**	C6H2Br4	634-89-9	3	1800	-10	0.139		
CEC	Galaxolide	C18H26O	1222-05-5	2	1837	-5	0.139		
CEC	Hexadecanenitrile	C16H31N	629-79-8	2	1895			15	0.102
CEC	Ethyl palmitate	C18H36O2	628-97-7	3	1991			21	0.186
CEC	Isopropyl palmitate	C19H38O2	142-91-6	3	2022	-6	0.040	6	0.002
CEC	Pentabromobenzene**	C6HBr5	608-90-2	2	2067	-12	0.016		
CEC	Methyl oleate	C19H36O2	112-62-9	3	2096			5	0.073
CEC	Ethyl stearate	C20H40O2	111-61-5	3	2192			21	0.186
CEC	Tributyl acetylcitrate	C20H34O8	77-90-7	2	2245			8	0.139
CEC	Di- <i>n</i> -hexyl phthalate	C20H30O4	84-75-3	2	2330			8	0.036
CEC	3,4',5,6'-Tetra- <i>tert</i> -butylbiphenyl-2,3'-diol*	C28H42O2	N/A	3	2345	-12	0.139	13	0.091
CEC	Butyl oleate	C22H42O2	142-77-8	3	2356			12	0.144
CEC	Hexabromobenzene**	C6Br6	87-82-1	2	2415	-12	0.010		
CEC	Di(2-ethylhexyl) phthalate	C24H38O4	117-81-7	3	2524			21	0.052
CEC	Bilobol dimethyl ether*	C23H38O2	22910-87-8	3	2624	-2	0.138		
CEC	Bis(diphenylmethyl) ether	C26H22O	574-42-5	2	2644	-3	0.037		
CEC	2-Ethylhexyl stearate	C26H52O2	22047-49-0	3	2697			13	0.099
CEC	β -Sitosterol acetate	C31H52O2	915-05-9	3	3068			5	0.128
HNP	2,4-Dibromoanisole**	C7H6Br2O	21702-84-1	3	1459	-8	0.089		
HNP	2,4,6-Tribromoanisole	C7H5Br3O	607-99-8	2	1605	3	0.144		
HNP	4-Bromoindole	C8H6BrN	52488-36-5	3	1618			-13	0.037
HNP	Q1	C9H3Cl7N2	428442-17-5	2	2121	-5	0.052	-3	0.016
HNP	Br ₄ Cl ₂ -MBP (+ co-eluting Br-TeCB)**	C12H5BrCl4	N/A	3	2316	6	0.177		
HNP	Br ₇ -MBP**	C9H3Br7N2	N/A	2	2793			-4	0.048
Terpene	Copaene	C15H24	3856-25-5	3	1375	-4	0.060	-6	0.016
Terpene	β -Neoclovene	C15H24	56684-96-9	3	1410	-5	0.128	-5	0.012
Terpene	(\pm)- β -Isocomene	C15H24	71596-72-0	3	1412			-8	0.004
Terpene	ϵ -Muurolene	C15H24	1136-29-4	3	1460			-4	0.186
Terpene	γ -Gurjunene	C15H24	22567-17-5	3	1474	1	0.186	-3	0.052
Terpene	Eremophilene	C15H24	10219-75-7	3	1494	-9	0.189		
Terpene	α -Muurolene	C15H24	10208-80-7	3	1497			-3	0.186
Terpene	Epizonarene	C15H24	41702-63-0	3	1503	8	0.139		
Terpene	β -Bisabolene	C15H24	495-61-4	3	1506	-4	0.177		
Terpene	Thujopsene-(12)	C15H24	N/A	3	1512			4	0.139

(continued on next page)

Table 1 (continued)

Class	Feature	Formula	CAS#	CL	LRI	Blue mussel soft body		Eelpout file	
						AC, %	p-value	AC, %	p-value
Terpene	γ -Cadinene	C15H24	39029-41-9	3	1512	3	0.139	-3	0.139
Terpene	Isopimaradiene	C20H32	1686-66-4	3	1995			-5	0.024
Terpene	Kaur-16-ene	C20H32	562-28-7	3	2042			-5	0.073
Terpenoid	Vanillin	C8H8O3	121-33-5	3	1390			-6	0.144
Terpenoid	2,2,4,4,7,7-Hexamethyloctahydro-1H-indene	C15H28	54832-83-6	3	1425			-7	0.002
Terpenoid	Geranylacetone	C13H22O	3796-70-1	3	1445	-8	0.052	11	0.001
Terpenoid	1,1,2,2,3,3-Hexamethylindane*	C15H22	91324-94-6	3	1456	9	0.073		
Terpenoid	Decahydro-1,1,4a,5,6-pentamethylnaphthalene	C15H28	80655-44-3	3	1463	5	0.089		
Terpenoid	Drimane	C15H28	5951-58-6	3	1473			-2	0.073
Terpenoid	cis-Calamenene	C15H22	483-77-2	3	1520			-4	0.052
Terpenoid	α -Calacorene	C15H20	21391-99-1	3	1541			-6	0.010
Terpenoid	Cadalene	C15H18	483-78-3	3	1670	-4	0.052	-2	0.102
Terpenoid	Neophytadiene	C20H38	504-96-1	3	1835			-1	0.102
Terpenoid	3-Methyl-2-(3,7,11-trimethyldodecyl) furan	C20H36O	166773-55-3	3	1913			-4	0.036
Terpenoid	Nordehydroabietane	C19H28	5323-56-8	3	1974	-5	0.102		
Terpenoid	18-Norabieta-8,11,13-triene	C19H28	N/A	3	2011	-7	0.139	-6	0.073
Terpenoid	Dehydroabietane	C20H30	19407-28-4	3	2050	-6	0.186	-1	0.139
Terpenoid	1,2,3,4,4a,9,10,10a-Octahydro-1,4a-dimethyl-7-(1-methylethyl)-1-phenanthrenol*	C19H28O	N/A	3	2176	-2	0.091		
Terpenoid	Squalene	C30H50	7683-64-9	3	2781			15	0.128

Abbreviations: CEC, contaminant of emerging concern; HNP, halogenated natural product; Q1, 2,3,3',4,4',5,5'-heptachloro-1'-methyl-1,2'-bipyrrrole; MBP, 1'-methyl-1,2'-bipyrrrole; OCP, organochlorine pesticide; PAH, polycyclic aromatic hydrocarbon; PBDE, polybrominated diphenyl ether; PCB, polychlorinated biphenyl; PCT, polychlorinated terphenyl.

* Compound identified using "non-hit" part of the EI workflow.

** Compound identified using the ECNI workflow.

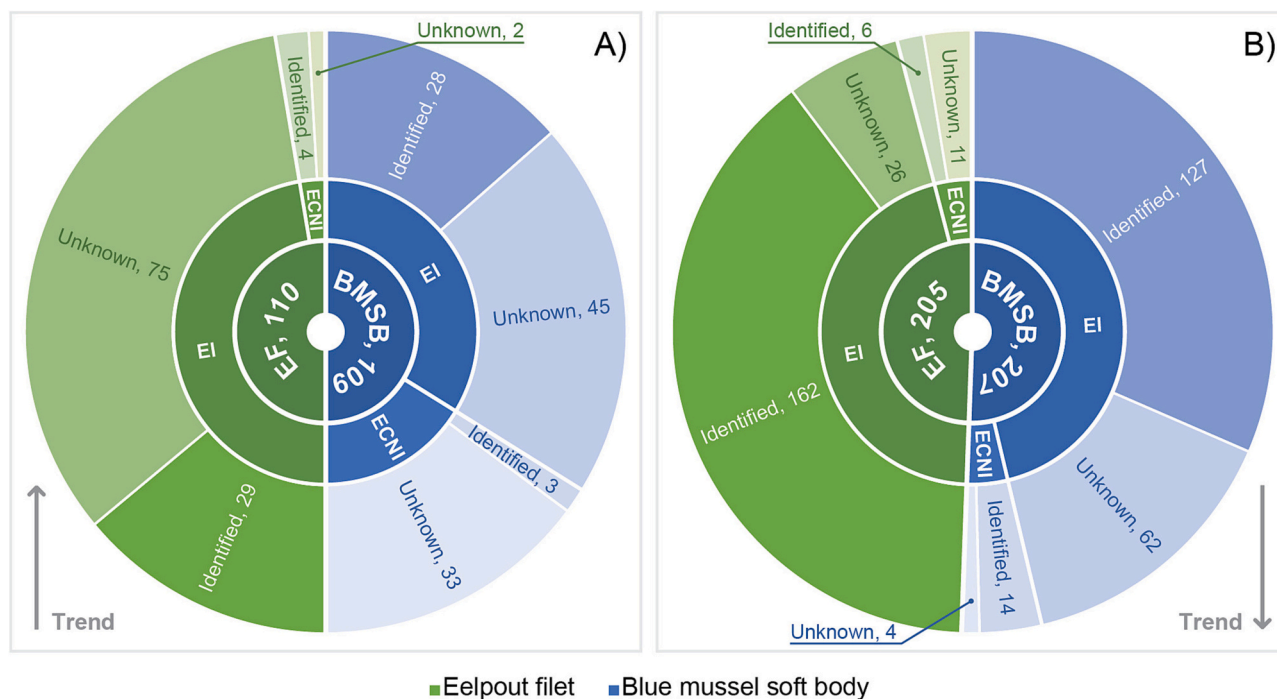


Fig. 2. An overview of the number of features that show increasing (A) and decreasing (B) temporal trends in samples of blue mussel and eelpout. Abbreviations: BMSB, blue mussel soft body; EF, eelpout file; EI, features detected in EI data; ECNI, brominated features detected in ECNI data.

sub-parts of the TT-NTS workflow, it was possible to find and tentatively identify 23 potential CECs in total (Table 1) at the German Baltic coastline: 10 personal care product (PCP) ingredients, two antioxidants, four brominated compounds used mostly as flame retardants in plastic production, four intermediates appearing during various industrial processes, and three compounds used in polymer production. Eleven of those compounds were found in blue mussel, all with decreasing

temporal trends, ranging from -12% to -2% , with a median AC value of -7% . Sixteen potential CECs were found in eelpout, all with increasing temporal trends, covering a range from $+3\%$ to $+21\%$. The median AC value of the eelpout samples was $+8\%$. Thus, the long-term data for the CECs showed decreasing temporal trends in blue mussels and increasing trends in eelpout. The German ESB sampling programme is highly standardized and no changes have been introduced to the

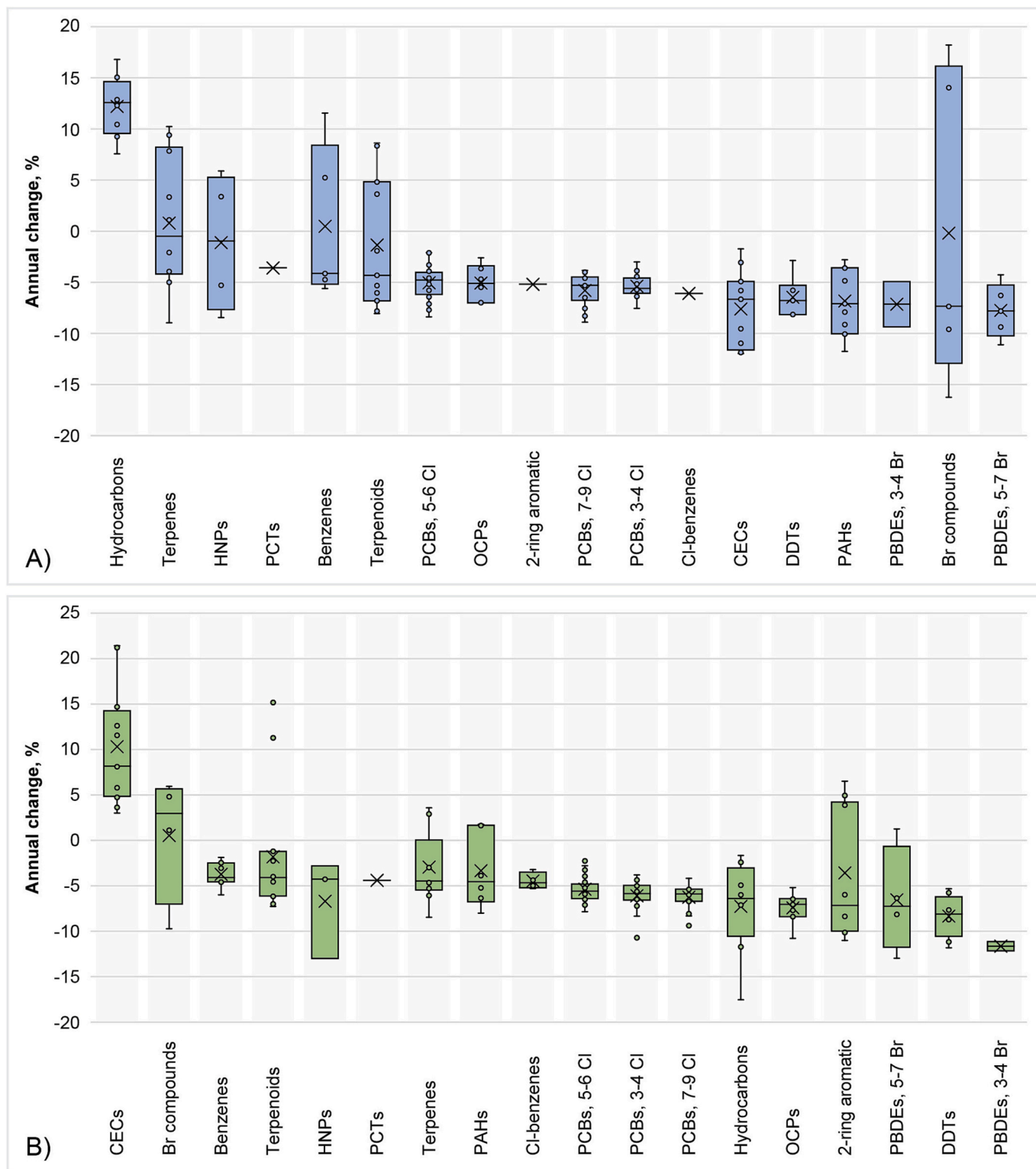


Fig. 3. An overview (box-and-whisker plot) of the features tentatively identified in the samples of blue mussel soft tissue (A) and eelpout filet (B). The features are arranged in order of decreasing (left to right) compound class median annual change (AC) for each species. Abbreviations: CECs, contaminants of emerging concern; HNPs, halogenated natural products; PCTs, polychlorinated terphenyls; PCBs, polychlorinated biphenyls; OCPs, organochlorine pesticides; PAHs, polycyclic aromatic hydrocarbons; PBDEs, polybrominated diphenyl ethers.

protocols for both blue mussel and eelpout. It is therefore hard to explain the difference in the temporal trends for the two species. Potential explanations for the contrasting temporal trends for CECs can be linked to several aspects, for example, to changes in eelpout migration pattern, food supply or feeding habits. In addition, to changes in size of both

species, *i.e.* Baltic eelpout individuals got slightly smaller ([German Environmental Specimen Bank, 2023c](#)), whereas blue mussels increased in size over the last years with a peak size in 2017 ([German Environmental Specimen Bank, 2023d](#)). This also explains the higher lipid content in the blue mussel samples from the recent years (Table S1 in the

SI). This fact can also mean that increase in size and lipid content dilutes the contaminants leading to the decreasing trends in blue mussel. Finally, a combination of the aforementioned factors and additional so far unknown factors can be the reason for the observed differences in the temporal trends. Another important aspect that explains the differences in temporal trends (in particular) and in contaminant profiles of blue mussel and eelpout (in general) to some extent is the difference in their metabolic systems, *i.e.* presence of cytochrome P450 system in eelpout and its absence in blue mussel. The enzymes of the cytochrome P450 family help metabolizing planar xenobiotic compounds, such as PCBs and PAHs, by inserting an oxygen atom into their molecules and making them more hydrophilic, hence, available for excretion with urine (Ronisz et al., 1999).

The PCP group contained seven compounds (here and in further passages of this sub-section, references refer to CEC use information when available) used as emollients in cosmetics, ethyl palmitate (Meijer et al., 2021), isopropyl palmitate (Larrañaga et al., 2016), ethyl stearate (Meijer et al., 2021), 2-ethylhexyl stearate (Meijer et al., 2021), methyl oleate (Meijer et al., 2021; Larrañaga et al., 2016), butyl oleate (Meijer et al., 2021; Larrañaga et al., 2016), and β -sitosterol acetate (von der Ohe and Aalizadeh, 2006), a fragrance ingredient galaxolide (hexahydrohexamethyl cyclopentabenzopyran, HHCb (Fan et al., 2019)), a UV screen benzophenone (Heffernan et al., 2015), and a surfactant 2,4,7,9-tetramethyl-5-decyn-4,7-diol (TMDD, frequently used in inkjet printer ink and various types of paints and coatings) (Hawley, 1977; ECHA, 2023b). Some of these compounds have various fields of application, for instance, ethyl palmitate and ethyl stearate are used as flavoring agents (Meijer et al., 2021), whereas methyl oleate and butyl oleate are also used as plasticizers (Larrañaga et al., 2016). Several of the compounds presented here may have both natural and anthropogenic origin *i.e.* β -sitosterol acetate and fatty acid esters, but since their industrial uses are increasing (see sub-section 3.6 and Fig. 5), we classified them as CECs.

Three of the PCPs were detected in blue mussel, all showing decreasing trends: benzophenone (AC -7%), isopropyl palmitate (-6%), and galaxolide (-5%). Nine out of 10 PCPs were detected in eelpout, all of which showed, in contrast to the blue mussel samples, increasing temporal trends: ethyl palmitate ($+21\%$), ethyl stearate ($+21\%$), butyl oleate ($+12\%$), 2-ethylhexyl stearate ($+13\%$), isopropyl palmitate ($+6\%$), β -sitosterol acetate ($+5\%$), methyl oleate ($+5\%$), benzophenone ($+4\%$), and 2,4,7,9-tetramethyl-5-decyn-4,7-diol ($+3\%$).

The antioxidants included 2,6-bis(1,1-dimethylethyl)phenol (Larrañaga et al., 2016) and 3,4',5,6'-tetra-*tert*-butylbiphenyl-2,3'-diol (Simcik et al., 2022). Both antioxidants were detected in blue mussel and showed decreasing trends (3,4',5,6'-tetra-*tert*-butylbiphenyl-2,3'-diol (-12%) and 2,6-bis(1,1-dimethylethyl)phenol (-6%)). The same two antioxidants were detected in eelpout with increasing trends: 3,4',5,6'-tetra-*tert*-butylbiphenyl-2,3'-diol ($+13\%$) and 2,6-bis(1,1-dimethylethyl)phenol ($+5\%$).

Four brominated compounds were tentatively identified: 1,2,4,5-tetrabromobenzene, 1,2,3,5-tetrabromobenzene, pentabromobenzene, and hexabromobenzene. All of them showed significant decreasing temporal trends in blue mussel samples with the following AC values: -12% for hexabromobenzene and pentabromobenzene, -11% for 1,2,4,5-tetrabromobenzene, and -10% for 1,2,3,5-tetrabromobenzene.

The intermediates included hexadecanenitrile (PubChem, 2023), 4-isopropoxyaniline (Plewe et al., 2021; Chen et al., 2023), bis(diphenylmethyl) ether (Mazid and Palmer, 1975), and bilobol dimethyl ether (1,3-dimethoxy-5-[(*Z*)-pentadec-8-enyl]benzene, (Nimgirawath et al., 1973; Tanaka et al., 2011)). Two intermediates were detected in blue mussel exhibiting decreasing temporal trends, namely, bis(diphenylmethyl) ether (-3%) and bilobol dimethyl ether (-2%). Another two intermediates showed increasing temporal trends in eelpout: hexadecanenitrile ($+15\%$) and 4-isopropoxyaniline ($+6\%$).

The compounds used in polymer production included two plastic

additives, di-*n*-hexyl phthalate (DnHP, (Meijer et al., 2021)) and di(2-ethylhexyl) phthalate (DEHP, (Meijer et al., 2021)), and one novel plasticizer tributyl acetyl citrate (acetyl tributyl citrate, ATBC, (García Ibarra et al., 2019)). Of these, none were found in blue mussel, whereas three compounds were detected in eelpout and showed increasing trends with AC values as follows: ATBC ($+8\%$), DnHP ($+8\%$), and DEHP ($+21\%$).

Most of the CECs that showed increasing trends are widely used in households (personal care products), various industrial processes (plastics additives) or are formed (intermediates) during them, which contributes to their increased release into the environment, explaining increasing temporal trends over recent decades.

Here, four CECs, namely, 2-ethylhexyl stearate, 1,2,3,5-tetrabromobenzene 4-isopropoxyaniline, and bilobol dimethyl ether, were reported, to the best of our knowledge, for the first time in marine biota samples. However, the identification accuracy of those should be verified using the appropriate reference standards that were not available at the time of the analysis of the samples.

3.4.2. Hydrocarbon-related compounds

3.4.2.1. Hydrocarbons. This class contains 11 tentatively identified compounds, namely, 1-hexylcyclohexene, 3-hexyl-1-cyclohexene, (3*E*)-3-tetradecene, 1-pentadecene, (2*Z*,4*E*)-3,7,11-trimethyl-2,4,10-dodecatriene, *trans*-1-methyl-2-nonyl-cyclohexane, (3*E*)-3-heptadecene, pristane (2,6,10,14-tetramethylpentadecane), 2-phytene (3,7,11,15-tetramethylhexadec-2-ene), phytadiene, and eicosadiene (isomer is not fully identified); see Table 1. Eight of these were detected in blue mussel, all of which exhibited increasing trends within a range from $+8\%$ to $+17\%$ with a median AC of $+13\%$ and the following individual AC values: $+17\%$ for 1-hexylcyclohexene, $+15\%$ for eicosadiene, $+13\%$ for (3*E*)-3-tetradecene and *trans*-1-methyl-2-nonyl-cyclohexane, $+12\%$ for 3-hexyl-1-cyclohexene, $+10\%$ for 1-pentadecene, $+9\%$ for (3*E*)-3-heptadecene, and $+8\%$ for pristane. In eelpout, eight compounds were detected, all of which showed, in contrast to the blue mussel, decreasing temporal trends within a range from -18% to -2% with a median AC of -7% : 1-hexylcyclohexene (-18%), 3-hexyl-1-cyclohexene (-12%), (2*Z*,4*E*)-3,7,11-trimethyl-2,4,10-dodecatriene (-7%), eicosadiene (-7%), (3*E*)-3-heptadecene (-6%), phytadiene (-5%), pristane (-2%), and 2-phytene (-2%). The increasing trends for hydrocarbons in blue mussels may indicate an increased use or release of oil products, whilst the decreasing trends for hydrocarbons in eelpout may be related to ecological factors.

3.4.2.2. Benzenes. Thirteen alkylbenzenes were tentatively identified: 1,2-diethyl-3,4-dimethylbenzene, 1,2,4-triethylbenzene, 1,1'-diphenylethane, (1-methylnonyl)benzene, (1-pentylhexyl)benzene, (1-butylheptyl)benzene, (1-propyloctyl)benzene, (1-pentylheptyl)benzene, (1-propylnonyl)benzene, (1-methylundecyl)benzene, (1-pentyldecyl)benzene, 1,3-dimethoxy-5-pentadecylbenzene, 1,3-dimethoxy-5-hexadecylbenzene (Table 1). Three showed decreasing temporal trends, namely, 1,2-diethyl-3,4-dimethylbenzene (-6%), 1,1'-diphenylethane (-5%), and 1,2,4-triethylbenzene (-4%), whereas two methoxylated alkylbenzenes exhibited increasing trends *i.e.* 1,3-dimethoxy-5-pentadecylbenzene ($+12\%$) and 1,3-dimethoxy-5-hexadecylbenzene ($+5\%$), in blue mussel; all were within a range from -6% to $+12\%$ with a median AC of $+4\%$. In eelpout, nine compounds, of which eight were unique, were found to show decreasing temporal trends: (1-pentyldecyl)benzene (-6%), (1-pentylheptyl)benzene (-5%), (1-propylnonyl)benzene (-5%), (1-pentylhexyl)benzene (-4%), (1-butylheptyl)benzene (-4%), (1-methylundecyl)benzene (-3%), (1-methylnonyl)benzene (-2%), (1-propyloctyl)benzene (-2%), and 1,2,4-triethylbenzene (-2%).

3.4.2.3. Two-ring aromatic compounds. This group contains compound classes with chemical structures that contain two aromatic rings. Ten

compounds were tentatively identified (Table 1): four naphthalenes (2-methylnaphthalene, 1-methylnaphthalene, 1,3-dimethylnaphthalene, 1,6-dimethylnaphthalene), five biphenyls (biphenyl, 2-ethylbiphenyl, 2,4'-dimethylbiphenyl, 2,2'-dimethylbiphenyl, 3,3'-dimethylbiphenyl), and dibenzofuran. All 10 compounds were detected in eelpout samples and were within a range from -11 % to +7 % with a median AC of -7 %. Of these, all the naphthalenes showed decreasing trends (2-methylnaphthalene (-11 %), 1,3-dimethylnaphthalene (-10 %), 1,6-dimethylnaphthalene (-10 %), and 1-methylnaphthalene (-8 %)) as well as biphenyl (-10 %) and dibenzofuran (-6 %), whereas 2-ethylbiphenyl, 2,4'-dimethylbiphenyl, and 2,2'-dimethylbiphenyl showed increasing trends with AC values of +7 %, +5 %, and +4 %, respectively. Only 2,2'-dimethylbiphenyl was detected in blue mussel, with a decreasing trend with AC value of -5 %.

3.4.2.4. Polycyclic aromatic hydrocarbons (PAHs). This class contains 11 tentatively identified PAHs with three to five aromatic rings, namely, anthracene, 1-methylphenanthrene, fluoranthene, pyrene, 9,9'-spirobifluorene, benzo[*e*]pyrene, perylene, *o*-terphenyl, *o,m*-quaterphenyl, *m,m*-quaterphenyl, and a methyl-anthracene/phenanthrene isomer (Table 1). Of these, 10 compounds were detected in blue mussel, all with decreasing temporal trends, ranging from -12 % to -3 % with a median AC of -8 %: benzo[*e*]pyrene (-12 %), 1-methylphenanthrene (-10 %), fluoranthene (-10 %), perylene (-9 %), *o*-terphenyl (-8 %), methyl-anthracene/methylphenanthrene (-7 %), anthracene (-5 %), *o,m*-quaterphenyl (-5 %), 9,9'-spirobifluorene (-3 %), and *m,m*-quaterphenyl (-3 %). In eelpout, six compounds were found and were within a range from -8 % to +2 % with a median AC of -5 %. Four of those had decreasing trends (pyrene (-8 %), *o*-terphenyl (-6 %), 9,9'-spirobifluorene (-5 %), and *o,m*-quaterphenyl (-4 %)), whereas two compounds showed increasing trends (1-methylphenanthrene (+2 %) and methylanthracene/methylphenanthrene (+2 %)).

3.4.3. Halogenated aromatic compounds

3.4.3.1. Chlorinated benzenes (Cl-benzenes). Four polychlorinated benzenes and octachlorostyrene were detected in the samples and all showed decreasing temporal trends (Table 1). Only 1,2,4,5-tetrachlorobenzene was detected in blue mussel and had an AC value of -6 %. Four other compounds were found in eelpout and were within a range from -5 % to -3 % with a median AC of -5 %, with the following individual AC values: -5 % for pentachlorobenzene and octachlorostyrene, -4 % for 1,2,3,4-tetrachlorobenzene, and -3 % for hexachlorobenzene.

3.4.3.2. Polychlorinated biphenyls (PCBs) and polychlorinated terphenyls (PCTs). A total of 84 features, which may potentially account for 99 PCB congeners as co-elution of two and three congeners may occur in several cases (see Table S2 in the SI), exhibited significant decreasing temporal trends in both blue mussel and eelpout. The assignment of the congeners was achieved by i) analysis of a 28-component PCB mixture (CL 1) and ii) using a RI database of the 209 PCBs developed in the course of previous studies (CL 2). The PCBs had annual change values in a range from -9 % to -2 % (median -5 %) in blue mussel and in a range from -11 % to -2 % (median -6 %) in eelpout. For full information on PCBs, please see Table S2 in the SI.

Two PCT congeners were tentatively identified: one tetrachloroterphenyls (Cl₄-terphenyl) and one dichloroterphenyl (Cl₂-terphenyl); see Table 1. The assignment of the exact structures was impossible due to the fact that the PCT class contains approximately 8, 500 possible congeners (Remberg et al., 1998). The two terphenyls showed decreasing temporal trends in blue mussel, both with AC value of -4 %. In eelpout, the Cl₂-terphenyl also showed a decreasing trend with the same AC value of -4 %.

3.4.3.3. Polybrominated diphenyl ethers (PBDEs). Eight PBDE congeners

were tentatively identified. All except one exhibited decreasing temporal trends (Table 1). In blue mussels, seven PBDEs had decreasing trends in a range from -11 % to -4 % (median -8 %), namely, BDE-100 (-11 %), BDE-47 (-9 %), BDE-182 (-9 %), BDE-99 (-8 %), BDE-154 with co-eluting brominated biphenyl 155 (-6 %), BDE-49 (-5 %), and BDE-153 (-4 %). As for the eelpout, the AC values were in a range from -13 % to +1 % (median -10 %): -13 % for BDE-99, -12 % for BDE-49, -11 % for BDE-47, -8 % for BDE-153, -6 % for BDE-100, and +1 % for BDE-155.

3.4.3.4. DDT and its metabolites. Eight compounds in this group were detected, all showing decreasing trends in both species (Table 1), which can be explained by international regulation of the use of parent compounds. In blue mussels, the AC values were the following (range from -8 % to -3 % and median of -7 %): AC -8 % for *p,p'*-DDD, *p,p'*-DDT, and *p,p'*-DDMS, -7 % for *o,p'*-DDE, -6 % for *p,p'*-DDMU, -5 % for *p,p'*-DDE, and -3 % for 1-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-2-chloroethylene. In eelpout, slightly stronger reductions were seen with median AC value of -8 % (range from -12 % to -5 %): AC -12 % for *p,p'*-DDD, -11 % for *p,p'*-DDT, -9 % for *p,p'*-DDMS and *o,p'*-DDMU, -8 % for *o,p'*-DDE and *p,p'*-DDMU, -6 % for *p,p'*-DDE, and -5 % for 1-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-2-chloroethylene.

3.4.3.5. Organochlorine pesticides (OCPs). As for the other pesticides and their metabolites, nine compounds showed decreasing temporal trends in the analyzed samples of blue mussel and eelpout (Table 1). Six OCPs were found in blue mussel with the following AC values (range from -7 % to -3 % and median AC -5 %): -7 % for *cis*-chlordane and *cis*-nonachlor, -5 % for β -hexachlorocyclohexane (β -HCH) and heptachlor epoxide, -4 % for *trans*-nonachlor, and -3 % for dieldrin. In eelpout, seven out of nine compounds were detected with median AC of -7 % (range from -11 % to -5 %): octachlor epoxide (-11 %), β -HCH (-8 %), *cis*-chlordane (-8 %), Parlar 40/41 (2-*endo*,3-*exo*,5-*endo*,6-*exo*,8b,9c,10a,10c-octachlorobornane/2-*exo*,3-*endo*,5-*exo*,8c,9b,9-*c*,10a,10b-octachlorobornane) (-7 %), *trans*-nonachlor (-6 %), *cis*-nonachlor (-6 %), and Parlar 26 (2-*endo*,3-*exo*,5-*endo*,6-*exo*,8b,8-*c*,10a,10c-octachlorobornane) (-5 %).

3.4.4. Halogenated natural products (HNPs)

Six HNPs, including five brominated and one chlorinated compounds, were identified in the samples, mostly showing decreasing trends (Table 1). Two of the compounds detected in blue mussel had decreasing trends (2,4-dibromoanisole (-8 %) and a fully-chlorinated methylbipyrrole Q1 (2,3,3',4,4',5,5'-heptachloro-1'-methyl-1,2'-bipyrrole) (-5 %)), whereas another two had increasing trends (2,4,6-tribromoanisole (+3 %) and Br₄Cl₂-MBP with co-eluting Br-TeCB (+6 %)) with a median AC value of -1 % (range from -8 % to +6 %). In eelpout, all the three detected HNPs showed decreasing trends with the following AC values (range from -13 % to -3 % and median AC of -4 %): -13 % for 4-bromoindole, -4 % for Br₇-MBP, and -3 % for Q1.

3.4.5. Terpenes and terpenoids

3.4.5.1. Terpenes. Terpenes consist of compounds of biogenic and anthropogenic origin with general formulae C₁₅H₂₄ (sesquiterpenes) and C₂₀H₃₂ (diterpenes). Thirteen compounds of this group were tentatively identified, seven in blue mussel and eight in eelpout (Table 1). In blue mussel, four compounds showed decreasing trends (eremophilene (-9 %), β -neoclovene (-5 %), β -bisabolene (-4 %), and copaene (-4 %)) and three had increasing trends (epizonarene (+8 %), γ -cadinene (+3 %), and γ -gurjunene (+1 %)) with a median AC value of -4 % (range from -9 % to +8 %). In eelpout, nine terpenes showed decreasing trends ((\pm)- β -Isocomene (-8 %), copaene (-6 %), β -neoclovene (-5 %), isopimaradiene (-5 %), kaur-16-ene (-5 %), ϵ -muurolene (-4 %), α -muurolene (-3 %), γ -gurjunene (-3 %), and γ -cadinene

(−3 %) and only one compound had an increasing trend (thujopsene-12) (+4 %)). The AC values were in a range from −8 % to +4 % and median of −5 %.

3.4.5.2. Terpenoids. Terpenoids include other isoprene derivatives, which often contain an oxygen atom. It was possible to detect and tentatively identify 16 terpenoids (Table 1). Eight such compounds were identified in blue mussel with the following AC values (range from −8 % to +9 % and median AC −5 %): geranylacetone (−8 %), 18-norabieta-8,11,13-triene (−7 %), dehydroabietane (−6 %), nordehydroabietane (−5 %), cadalene (−4 %), 1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-7-(1-methylethyl)-1-phenanthrenol (−2 %), decahydro-1,1,4a,5,6-pentamethylnaphthalene (+5 %), and 1,1,2,2,3,3-hexamethylindane (+9 %). In eelpout, 12 terpenoids were detected, of which 10 showed decreasing trends (2,2,4,4,7,7-hexamethyloctahydro-1H-indene (−7 %), vanillin (−6 %), α -calacorene (−6 %), 18-norabieta-8,11,13-triene (−6 %), 3-methyl-2-(3,7,11-trimethyl)dodecyl) furan (−4 %), drimane (−4 %), *cis*-calamenene (−2 %), cadalene (−2 %), dehydroabietane (−1 %), and neophytadiene (−1 %)) and two showed increasing trends (geranylacetone (+11 %) and squalene (+15 %)) with a median AC of −3 % (range from −2 % to +15 %).

3.4.6. Compounds assigned molecular formula (CL 4 features)

A total of 26 features make up this group; see Table S3 in the SI. For most features, it was not possible to assign a compound class, but 11 features could be assigned to four different classes. The temporal trends of these resembled those of the tentatively identified compounds that belong to the same class (Table 1).

One hydrocarbon with formula $C_{19}H_{34}$ was detected and had an increasing temporal trend (AC +12 %) in blue mussel and decreasing trend (−5 %) in eelpout, whereas one 6-ring PAH ($C_{24}H_{14}$) had a decreasing trend in blue mussel with an AC value of −4 %.

Four terpenes with general formulae $C_{15}H_{24}$ were detected in both blue mussel and eelpout. In blue mussel, two of the detected terpenes had increasing trends (AC values of +9 % and +10 %) and one had a decreasing trend (−2 %). As for the eelpout samples, two terpenes showed increasing (both +3 %) and one decreasing (−6 %) trends.

Five terpenoids were also found to show temporal trends in the samples under study. Three of these were found in blue mussel with the following AC values: +8 % for a compound with a formula $C_{15}H_{22}$, +4 % for another $C_{15}H_{22}$, and −8 % for a compound with formula $C_{14}H_{20}O_3$. In eelpout samples, three terpenoids showed decreasing trends: $C_{15}H_{26}$ (−7 %), $C_{14}H_{20}O_3$ (−7 %), and $C_{20}H_{30}$ (−1 %).

The remaining CL 4 features included 15 unclassified compounds with various temporal trends (Table S3 in the SI). Of these, 10 were detected in blue mussel (median AC value of +4 %) and eight were found in eelpout (median AC of −5 %).

3.4.7. Brominated and iodinated organic compounds with unknown chemical structure

A number of compounds were exhaustively fragmented by the dissociative electron capture process in ECNI and only halogen ions were detected. This was particularly true for iodinated compounds, which have an especially weak bond between carbon and iodine (Kerr, 1966). These brominated and iodinated features were distinguished by the type of halogen substitution and the retention time, and were assigned identification confidence level 5 (CL 5), see Table S4 in the SI.

The CL 5 feature group contained nine brominated compounds, of which five were detected in blue mussel and four in eelpout. The median AC value for the brominated compounds found in blue mussel was −7 %, whereas an AC +3 % was observed for those found in eelpout (Table S4 in the SI).

In addition, a plethora of organoiodine compounds was observed during processing of ECNI data. Examples of iodine extracted ion chromatograms (m/z 126.9045) of the three Florisil® fractions of a blue

mussel sample are given in Fig. S1 in the SI. This class of compounds has attracted increasing attention in recent years. A review of naturally occurring organoiodines has been published (Wang et al., 2014) and it includes approximately 180 compounds in various biotic and abiotic samples. Another study described a development of an NTS method that allowed determination of molecular formulae for almost 3000 natural and synthetic organoiodine compounds in sediments (Peng et al., 2016).

In total, 134 iodine containing features were found to have significant temporal trends in blue mussel and eelpout (see Table S4 in the SI). In blue mussel, 69 features were detected with the median AC value of +4 % (range from −23 % to +22 %), of which 37 features showed increasing and 32 features decreasing trends. In eelpout, 73 features were detected with the median AC value of +7 % (range from −12 % to +16 %), of which 53 features showed increasing and 20 features decreasing trends. Thus, more than half of features (around 54 % for blue mussel and around 73 % for eelpout) showed increasing temporal trends. The AC frequency distribution is shown in Fig. 4.

It would be interesting to characterize the many compounds that show increasing temporal trends in eelpout further e.g. using soft ionization techniques. The feasibility of LC-MS/MS to enable acquisition of molecular ion information has already been demonstrated by Peng et al. (2016) (Peng et al., 2016). Another way would be to analyze the samples using GC×GC-MS in low-energy EI mode, which may separate organoiodines from other more abundant compounds and also generate some molecular ions.

3.5. Temporal trends comparison

In the following sub-section, the temporal trends (characterized by annual change (AC) values, %) of a number of POPs identified in this work are compared with AC values retrieved from scientific studies targeting the same analytes and species in the southwestern Baltic Sea. The comparisons were made to ensure that the AC values obtained using the developed TT-NTS workflow closely match previously reported values and, thus, that the workflow gives reliable results. The time-trend comparison is summarized in Table 2. A number of studies of legacy contaminants have been carried out in the area, but, unfortunately, it was not possible to find any matching time-trend data for CECs and HNPBs in blue mussels and eelpout.

The overall differences between the studies were evaluated using the ratios of $AC_{\text{ThisStudy}}(\text{POP}) : AC_{\text{Literature}}(\text{POP})$ and associated relative standard deviation (RSD) values. The average difference and RSD between the values reported here and in the literature were 1.4 and 70 %, respectively. Species-wise, the deviation in eelpout data was smaller than in blue mussel data: ratio 1.4 with RSD 47 % vs. 1.5 and 85 %, respectively. Considering that most of the comparison data was from the Swedish south-east coast (Kväddöfjärden) and the study samples from the central part of the German Baltic Sea coast, the agreement can be considered to be good. The high similarity between the datasets was further manifested in greatly overlapping AC ranges for both blue mussel soft body (−4 % to −12 % (this study) vs. −2 % to −21 % (literature data)) and eelpout file (−3 % to −13 % (this study) vs. −2 % to −9 % (literature data)).

Nyberg et al. (2015) (Nyberg et al., 2015) reported AC values for two PCBs, *p,p'*-DDE and β -hexachlorocyclohexane (β -HCH) in blue mussel and eelpout. AC values for blue mussel reported here were in good agreement with values from Nyberg et al. (ratio of 1.2 and RSD of 20 %): −4 % (this study) vs. −3 % (literature) for CB-153, −4 % (this study) vs. −4 % (literature) for CB-118, −5 % (this study) vs. −4 % (literature) for *p,p'*-DDE, and −5 % (this study) vs. −6 % (literature) for β -HCH. For eelpout, the overall ratio was 0.9 and RSD 51 % with individual AC values as follows: −5 % (this study) vs. −9 % (literature) for CB-153, −5 % (this study) vs. −8 % (literature) for CB-118, −6 % (this study) vs. −8 % (literature) for *p,p'*-DDE, and −8 % (this study) vs. −5 % (literature) for β -HCH.

The values from the report by Soerensen and Faxneld (2022) for a

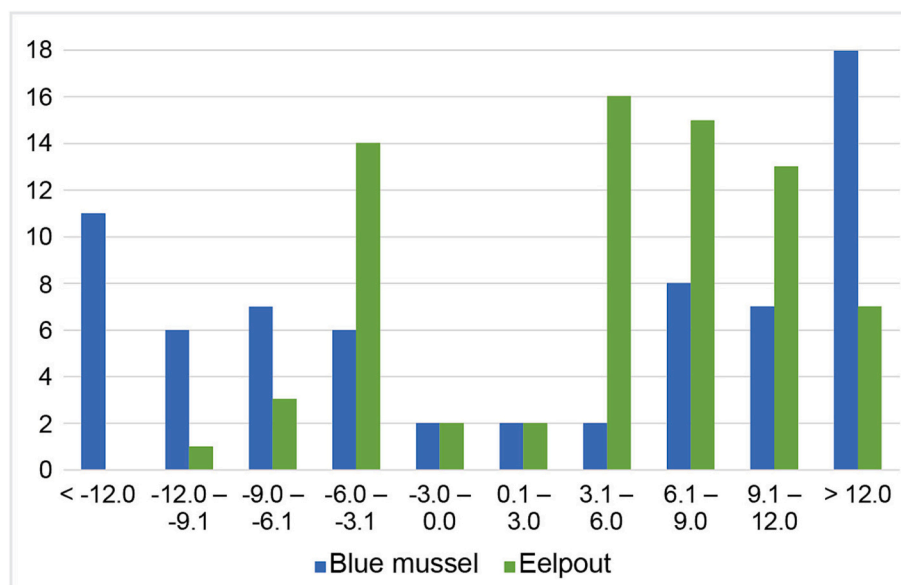


Fig. 4. Annual change (in %) frequency distribution histogram for organoiodine features in blue mussel (blue) and eelpout (green) samples.

number of OCPs, PCBs, and PBDEs in blue mussel were approximately one-and-a-half times lower on average in comparison to the AC values reported here (ratio of 1.9 with RSD 86 %; Table 2), although identical values were observed for *p,p'*-DDE (−5 %), *p,p'*-DDD (−8 %), and CB-153 (−4 %). The biggest discrepancies were observed for the two PAHs and BDE-100: −10 % (this study) vs. −2 % (literature) for fluoranthene, −5 % vs. −2 % for anthracene, and −11 % vs. −6 % for BDE-100. As for the eelpout, AC values for five PCBs, four OCPs, and two PBDEs were compared, resulting in the average ratio of 1.2 and RSD 44 % (Table 2). The best agreement was for PCBs with two identical AC values for CB-180 (−6 % for both studies) and CB-118 (−5 %).

Last, the annual concentrations for a number of POPs detected in this work were retrieved from the German ESB data search page (German Environmental Specimen Bank, 2023e) and used to calculate AC values in the same manner as was done for the data of this study (Table 2). Seven compounds showed statistically significant trends in blue mussel (ratio of 1.0 and RSD of 52 %), with AC values as follows: −5 % (this study) vs. −7 % (literature) for BDE-49, −11 % vs. −6 % for BDE-100, −4 % vs. −6 % for BDE-153, −6 % vs. −7 % for BDE-154, −5 % vs. −21 % for galaxolide, −10 % vs. −6 % for fluoranthene, and −12 % vs. −11 % for benzo[*e*]pyrene. In eelpout, AC values of 11 compounds were compared resulting in a ratio of 1.6 with RSD 41 % and the following individual values: −6 % (this study) vs. −4 % (literature) for CB-180, −5 % vs. −2 % for CB-153, −5 % vs. −5 % for CB-138, −6 % vs. −3 % for *p,p'*-DDE, −12 % vs. −4 % for *p,p'*-DDD, −8 % vs. −7 % for β -HCH, −11 % vs. −8 % for BDE-47, −13 % vs. −7 % for BDE-99, −6 % vs. −7 % for BDE-100, and −8 % vs. −8 % for BDE-153.

3.6. Prioritization of compounds with increasing trends

For the features that were tentatively identified and showed increasing temporal trends, relative abundance values (RA, in %) were calculated relative to legacy contaminants (reference compounds). The ones that exceed or are close to the levels of the reference compounds and at the same time demonstrate strongly increasing temporal trends might be prioritized for further risk assessment and subsequent chemical management and emission control actions.

The RA were calculated according to the following equation:

$$RA = \frac{RR(L.w.)_{Cpd}}{RR(L.w.)_{Ref}} \times 100\% \quad (1)$$

The average lipid weight normalized relative response of the compound ($\overline{RR(L.w.)_{Cpd}}$) and the reference compound ($\overline{RR(L.w.)_{Ref}}$), respectively, was calculated across all years for a given species. CB-153 was chosen as a reference compound for EI data and BDE-99 was chosen for ECNI data, due to their high abundance in the species under study and high response and identification confidence in EI and ECNI, respectively.

Sixty-two compounds showed increasing trends, of which 43 compounds were identified at CL 3 or CL 2 (Table 3). In the blue mussel samples, only one unidentified hydrocarbon with formula $C_{19}H_{34}$ and two unknown brominated compounds Br_Cpd_31.938 and Br_Cpd_30.411 showed RAs considerably higher than CB-153 or BDE-99: 260 %, 54,000 %, and 150,000 %, respectively. It was possible to assign only a tentative formula to the hydrocarbon, which was detected in EI mode (Fig. S2A in the SI). However, the identities of brominated compounds remained unresolved as their ECNI spectra contained only Br ions (Fig. S2B–C in the SI). The EI spectra at the corresponding retention times were examined in an attempt to tentatively identify the two brominated compounds, but without success. All of these have AC values above 10 %. Given the high RA % and AC % of the two brominated compounds those features should be prioritized for further identification work. As for the eelpout, seven features with increasing temporal trends were present at levels higher than CB-153. Three were hydrocarbons, squalene (154 %), methylanthracene/methylphenanthrene (180 %), and unknown compound (21,000 %), whose formula ($C_{15}H_{28}$) was tentatively assigned based on its mass spectrum (Fig. S2D in the SI). The remaining four were CECs: methyl oleate (310 %), 2,4,7,9-tetramethyl-5-decyn-4,7-diol (TMDD, 1,300 %), di-*n*-hexyl phthalate (DnHP, 2,200 %), and hexadecanenitrile (3,300 %). Within this compound class we also found four compounds at levels around 10 % of that of CB-153: ethyl palmitate (16 %), ethyl stearate (11 %), butyl oleate (12 %) and di(2-ethylhexyl) phthalate (12 %). All of these have strongly increasing temporal trends with AC values exceeding 10 % (Table 3).

Thus, altogether eight CECs occur at levels exceeding, or slightly below, that of CB-153 and have increasing or strongly increasing temporal trends. These included four PCPs: methyl oleate (RA 310 %, AC 5 %), ethyl palmitate (RA 16 %, AC 21 %), ethyl stearate (RA 11 %, AC 21 %), and butyl oleate (RA 12 %, AC 12 %), which all are used as emollients. This group of compounds may deserve further attention. In addition, the three compounds with the highest abundance relative to CB-153, i.e. hexadecanenitrile (RA 3,300 %, AC 15 %), DnHP (RA 2,200 %, AC 8 %), and TMDD (RA 1,300 %, AC 3 %), may also be prioritized

Table 2

Compilation of annual change information for selected organic pollutants identified in this study and literature data.

Species & tissue	Time span	Location	Feature	Annual change, %			
				This study*	Literature	Ratio	Literature reference
Blue mussel soft body	1995–2012	Kvädöfjärden	CB-153	-4	-3	1.3	Nyberg et al., 2015
Blue mussel soft body	1995–2012	Kvädöfjärden	CB-118	-4	-4	1.0	Nyberg et al., 2015
Blue mussel soft body	1995–2012	Kvädöfjärden	<i>p,p'</i> -DDE	-5	-4	1.5	Nyberg et al., 2015
Blue mussel soft body	1996–2012	Kvädöfjärden	β -HCH	-5	-6	0.9	Nyberg et al., 2015
Blue mussel soft body	1995–2020	Kvädöfjärden	CB-153	-4	-4	0.9	Soerensen and Faxnel, 2022
Blue mussel soft body	1995–2020	Kvädöfjärden	CB-118	-4	-5	0.8	Soerensen and Faxnel, 2022
Blue mussel soft body	1995–2020	Kvädöfjärden	<i>p,p'</i> -DDT	-8	-4	2.2	Soerensen and Faxnel, 2022
Blue mussel soft body	1995–2020	Kvädöfjärden	<i>p,p'</i> -DDE	-5	-5	1.1	Soerensen and Faxnel, 2022
Blue mussel soft body	1995–2020	Kvädöfjärden	<i>p,p'</i> -DDD	-8	-8	1.0	Soerensen and Faxnel, 2022
Blue mussel soft body	1996–2020	Kvädöfjärden	β -HCH	-5	-7	0.8	Soerensen and Faxnel, 2022
Blue mussel soft body	2000–2020	Kvädöfjärden	BDE-47	-9	-6	1.5	Soerensen and Faxnel, 2022
Blue mussel soft body	2000–2020	Kvädöfjärden	BDE-99	-8	-7	1.1	Soerensen and Faxnel, 2022
Blue mussel soft body	2000–2020	Kvädöfjärden	BDE-100	-11	-6	1.8	Soerensen and Faxnel, 2022
Blue mussel soft body	1987–2020	Kvädöfjärden	Anthracene	-5	-2	2.8	Soerensen and Faxnel, 2022
Blue mussel soft body	1987–2020	Kvädöfjärden	Fluoranthene	-10	-2	6.6	Soerensen and Faxnel, 2022
Blue mussel soft body	1996–2015	Darßer Ort	BDE-49	-5	-7	0.7	German ESB data**
Blue mussel soft body	1996–2015	Darßer Ort	BDE-100	-11	-6	1.8	German ESB data**
Blue mussel soft body	1996–2015	Darßer Ort	BDE-153	-4	-6	0.7	German ESB data**
Blue mussel soft body	1996–2015	Darßer Ort	BDE-154	-6	-7	0.9	German ESB data**
Blue mussel soft body	1994–2000	Darßer Ort	Galaxolide	-5	-21	0.2	German ESB data**
Blue mussel soft body	1994–2017	Darßer Ort	Fluoranthene	-10	-6	1.7	German ESB data**
Blue mussel soft body	1994–2017	Darßer Ort	Benzo[e]pyrene	-12	-11	1.1	German ESB data**
Eelpout filet	1995–2012	Kvädöfjärden	CB-153	-5	-9	0.6	Nyberg et al., 2015
Eelpout filet	1995–2012	Kvädöfjärden	CB-118	-5	-8	0.7	Nyberg et al., 2015
Eelpout filet	1995–2012	Kvädöfjärden	<i>p,p'</i> -DDE	-6	-8	0.7	Nyberg et al., 2015
Eelpout filet	1995–2012	Kvädöfjärden	β -HCH	-8	-5	1.8	Nyberg et al., 2015
Eelpout filet	1995–2020	Kvädöfjärden	CB-180	-6	-6	1.0	Soerensen and Faxnel, 2022
Eelpout filet	1995–2020	Kvädöfjärden	CB-153	-5	-6	0.9	Soerensen and Faxnel, 2022
Eelpout filet	1995–2020	Kvädöfjärden	CB-118	-5	-5	1.0	Soerensen and Faxnel, 2022
Eelpout filet	1995–2020	Kvädöfjärden	CB-101	-3	-5	0.6	Soerensen and Faxnel, 2022
Eelpout filet	1995–2020	Kvädöfjärden	<i>p,p'</i> -DDT	-11	-5	2.5	Soerensen and Faxnel, 2022
Eelpout filet	1995–2020	Kvädöfjärden	<i>p,p'</i> -DDE	-6	-6	0.9	Soerensen and Faxnel, 2022
Eelpout filet	1995–2020	Kvädöfjärden	<i>p,p'</i> -DDD	-12	-8	1.4	Soerensen and Faxnel, 2022
Eelpout filet	1995–2020	Kvädöfjärden	HCB	-3	-2	2.0	Soerensen and Faxnel, 2022
Eelpout filet	1999–2020	Kvädöfjärden	BDE-47	-11	-9	1.2	Soerensen and Faxnel, 2022
Eelpout filet	1999–2020	Kvädöfjärden	BDE-100	-6	-7	1.0	Soerensen and Faxnel, 2022
Eelpout filet	1994–2017	Darßer Ort	CB-180	-6	-4	1.5	German ESB data**
Eelpout filet	1994–2017	Darßer Ort	CB-153	-5	-2	2.5	German ESB data**
Eelpout filet	1994–2017	Darßer Ort	CB-138	-5	-5	1.0	German ESB data**
Eelpout filet	1994–2017	Darßer Ort	<i>p,p'</i> -DDE	-6	-3	2.0	German ESB data**
Eelpout filet	1994–2017	Darßer Ort	<i>p,p'</i> -DDD	-12	-4	3.0	German ESB data**
Eelpout filet	1994–2017	Darßer Ort	β -HCH	-8	-7	1.2	German ESB data**
Eelpout filet	2003–2017	Darßer Ort	BDE-47	-11	-8	1.4	German ESB data**
Eelpout filet	2003–2017	Darßer Ort	BDE-99	-13	-7	1.9	German ESB data**
Eelpout filet	2003–2017	Darßer Ort	BDE-100	-6	-7	0.9	German ESB data**
Eelpout filet	2003–2017	Darßer Ort	BDE-153	-8	-8	1.0	German ESB data**

Abbreviations: (P)CB, (poly)chlorinated biphenyl; HCH, hexachlorocyclohexane; BDE, brominated diphenyl ether; HCB, hexachlorobenzene.

* Samples of this study were collected in Darßer Ort between 1994 and 2017 and compared to the studies from locations close by when possible. For more information on the samples of this study please see Table S1 in the SI.

** Annual change values were calculated in the same way as for this study using the yearly concentrations provided at the Data search page of the German ESB webpage, https://www.umweltprobenbank.de/en/documents/investigations/specimen_types?genders=0. The retrieved concentrations were in ng/g of fresh weight, then, the responses were normalized to 1 g of lipids using provided lipid content.

due to their high abundance and moderate to high annual increase.

The prioritized chemicals high RA values and increasing AC values were mostly in good agreement with use information (Fig. 5), which was generated using chemicalstripes, an R package that retrieves data from PubChem and creates a stripe plot showing the number of patents filed or references published for a given compound over time (Aurich et al., 2023a; Aurich et al., 2023b). An excellent agreement between RA/AC values and use information was observed for ethyl palmitate (Fig. 5A), methyl oleate (Fig. 5B), and TMDD (Fig. 5C). This can be explained by the fact that those three compounds are used as PCPs or solvents with the first two being the so-called “down-the-drain” chemicals, which are almost immediately released into the environment. On the other hand, DnHP (Fig. 5D) is used as a plasticizer and will, therefore, be released from consumer articles and building materials by gaseous and particulate emissions over extended periods of time, resulting in a delay in peak environmental concentration. This can explain the fact that the highest

number of patents/references was found for year 2002 (Fig. 5D), shortly after the phasing out of DEHP had started in Europe (EC, 1999), whilst an increasing temporal trend and a high RA were still observed in 2017 (Table 3). Finally, hexadecanenitrile (Fig. 5E) is an intermediate used or formed in various processes, which may explain the uneven stripe plot, increasing trend, and high relative abundance (Table 3).

4. Conclusions

In this study, we present long-term (23 years) data on temporal trends of chlorinated, brominated, iodinated, and non-halogenated organic contaminants in Baltic blue mussel and eelpout.

This work utilized an improved version of the previously published fast and highly automated NTS data processing workflow that allows for detection and identification of various classes of lipophilic organic contaminants. In particular, the ECNI data processing was further

Table 3

Annual changes (ACs), relative abundances (RAs), formulae, CAS#, identification confidence levels (CLs), and linear retention indices (LRIs) for the tentatively identified compounds with significant increasing temporal trends ($p \leq 0.2$) in samples of blue mussel (soft body) and eelpout (filet).

Class	Feature	Formula	CAS#	CL	LRI	Blue mussel soft body		Eelpout filet	
						AC, %	RA*, %	AC, %	RA, %
Hydrocarbon	3-Hexyl-1-cyclohexene	C12H22	15232-78-7	3	1231	12	57		
Hydrocarbon	1-Hexylcyclohexene	C12H22	3964-66-7	3	1241	17	33		
Hydrocarbon	(3E)-3-Tetradecene	C14H28	41446-68-8	3	1386	13	51		
Hydrocarbon	1-Pentadecene	C15H30	13360-61-7	3	1480	10	5		
Hydrocarbon	<i>trans</i> -1-Methyl-2-nonyl-cyclohexane**	C16H32	N/A	3	1586	13	47		
Hydrocarbon	(3E)-3-Heptadecene	C17H34	68155-00-0	3	1682	9	29		
Hydrocarbon	Pristane	C19H40	1921-70-6	3	1705	8	53		
Hydrocarbon	C19H34**	C19H34	N/A	4	1859	12	260		
Hydrocarbon	Eicosadiene	C20H38	N/A	3	1878	15	11		
Benzene	1,3-Dimethoxy-5-pentadecylbenzene	C23H40O2	23032-48-6	3	2647	12	38		
Benzene	1,3-Dimethoxy-5-hexadecylbenzene**	C24H42O2	N/A	3	2711	5	1.1		
2-ring aromatic	2-Ethylbiphenyl**	C14H14	1812-51-7	3	1489			7	8
2-ring aromatic	2,4'-Dimethylbiphenyl	C14H14	1166-18-3	3	1503			5	3
2-ring aromatic	2,2'-Dimethylbiphenyl	C14H14	605-39-0	3	1537			4	66
2-ring aromatic	3,3'-Dimethylbiphenyl	C14H14	612-75-9	3	1587			4	8
PAH	Methylanthracene/methylphenanthrene	C15H12	N/A	3	1892			2	180
PAH	1-Methylphenanthrene	C15H12	832-69-9	3	1909			2	16
PBDE	BDE-155**	C12H4Br6O	35854-94-5	2	2853			1	22
CEC	4-Isopropoxyaniline	C9H13NO	7664-66-6	3	1316			6	5
CEC	2,4,7,9-Tetramethyl-5-decyn-4,7-diol	C14H26O2	126-86-3	3	1405			3	1,300
CEC	2,6-Bis(1,1-dimethylethyl)phenol	C14H22O	128-39-2	2	1430			5	0.2
CEC	Benzophenone	C13H10O	119-61-9	2	1624			4	0.4
CEC	Hexadecanenitrile	C16H31N	629-79-8	2	1895			15	3,300
CEC	Ethyl palmitate	C18H36O2	628-97-7	3	1991			21	16
CEC	Isopropyl palmitate	C19H38O2	142-91-6	3	2022			6	0.6
CEC	Methyl oleate	C19H36O2	112-62-9	3	2096			5	310
CEC	Ethyl stearate	C20H40O2	111-61-5	3	2192			21	11
CEC	Tributyl acetylacrylate	C20H34O8	77-90-7	2	2245			8	8
CEC	Di- <i>n</i> -hexyl phthalate	C20H30O4	84-75-3	2	2330			8	2,200
CEC	3,4',5,6'-Tetra- <i>tert</i> -butylbiphenyl-2,3'-diol**	C28H42O2	N/A	3	2345			13	1.3
CEC	Butyl oleate	C22H42O2	142-77-8	3	2356			12	12
CEC	Di(2-ethylhexyl) phthalate	C24H38O4	117-81-7	3	2524			21	12
CEC	2-Ethylhexyl stearate	C26H52O2	22047-49-0	3	2697			13	1.3
CEC	β -Sitosterol acetate	C31H52O2	915-05-9	3	3068			5	0.3
HNP	2,4,6-Tribromoanisole	C7H5Br3O	607-99-8	2	1605	3	1.4		
HNP	Br4Cl2-MBP (+ co-eluting Br-TeCB)**	C12H5BrCl4	N/A	3	2316	6	40		
Terpene	C15H24**	C15H24	N/A	4	1307	9	17		
Terpene	C15H24**	C15H24	N/A	4	1309	10	19	3	17
Terpene	C15H24	C15H24	N/A	4	1502			3	0.6
Terpene	Epizonarene	C15H24	41702-63-0	3	1503	8	55		
Terpene	γ -Cadinene	C15H24	39029-41-9	3	1512	3	4		
Terpene	γ -Gurjunene	C15H24	22567-17-5	3	1474	1	5		
Terpene	Thujopsene-(I2)	C15H24	N/A	3	1512			4	4
Terpenoid	Geranylacetone	C13H22O	3796-70-1	3	1445			11	32
Terpenoid	1,1,2,2,3,3-Hexamethylindane**	C15H22	91324-94-6	3	1456	9	21		
Terpenoid	Decahydro-1,1,4a,5,6-pentamethylnaphthalene	C15H28	80655-44-3	3	1463	5	4		
Terpenoid	C15H22**	C15H22	N/A	4	1463	8	14		
Terpenoid	C15H22**	C15H22	N/A	4	1535	4	5		
Terpenoid	Squalene	C30H50	7683-64-9	3	2781			15	150
CL 4 (other)	C15H28	C15H28	N/A	4	1236	10	19		
CL 4 (other)	C15H28	C15H28	N/A	4	1260	7	79		
CL 4 (other)	C15H28**	C15H28	N/A	4	1311	4	9	8	21,000
CL 4 (other)	C15H28**	C15H28	N/A	4	1312	5	11		
CL 4 (other)	C14H26**	C14H26	N/A	4	1338	10	4		
CL 4 (other)	C8H8O3	C8H8O3	N/A	4	1390	2	47		
CL 4 (other)	C15H16**	C15H16	N/A	4	1647	9	7		
CL 4 (other)	C20H28	C20H28	N/A	4	1914			15	5
Br compound	Br_Cpd_18.591***	Unknown	N/A	5	1580			1.0	74
Br compound	Br_Cpd_30.411***	Unknown	N/A	5	2031	18	150,000		
Br compound	Br_Cpd_31.938***	Unknown	N/A	5	2093	14	54,000		
Br compound	Br_Cpd_42.625***	Unknown	N/A	5	2582			5	24
Br compound	Br_Cpd_43.235***	Unknown	N/A	5	2614			6	53

Abbreviations: PAH, polycyclic aromatic hydrocarbon; PBDE, polybrominated diphenyl ether; CEC, contaminant of emerging concern; HNP, halogenated natural product; MBP, 1'-methyl-1,2'-bipyrrole; TeCB, tetrachlorinated biphenyl; Br_Cpd, organobromine compound.

* RA values were calculated relative to legacy contaminants (reference compounds): CB-153 was chosen for EI data and BDE-99 was chosen for ECNI data.

** Compound identified using "non-hit" part of the EI workflow.

*** Compound identified using the ECNI workflow.

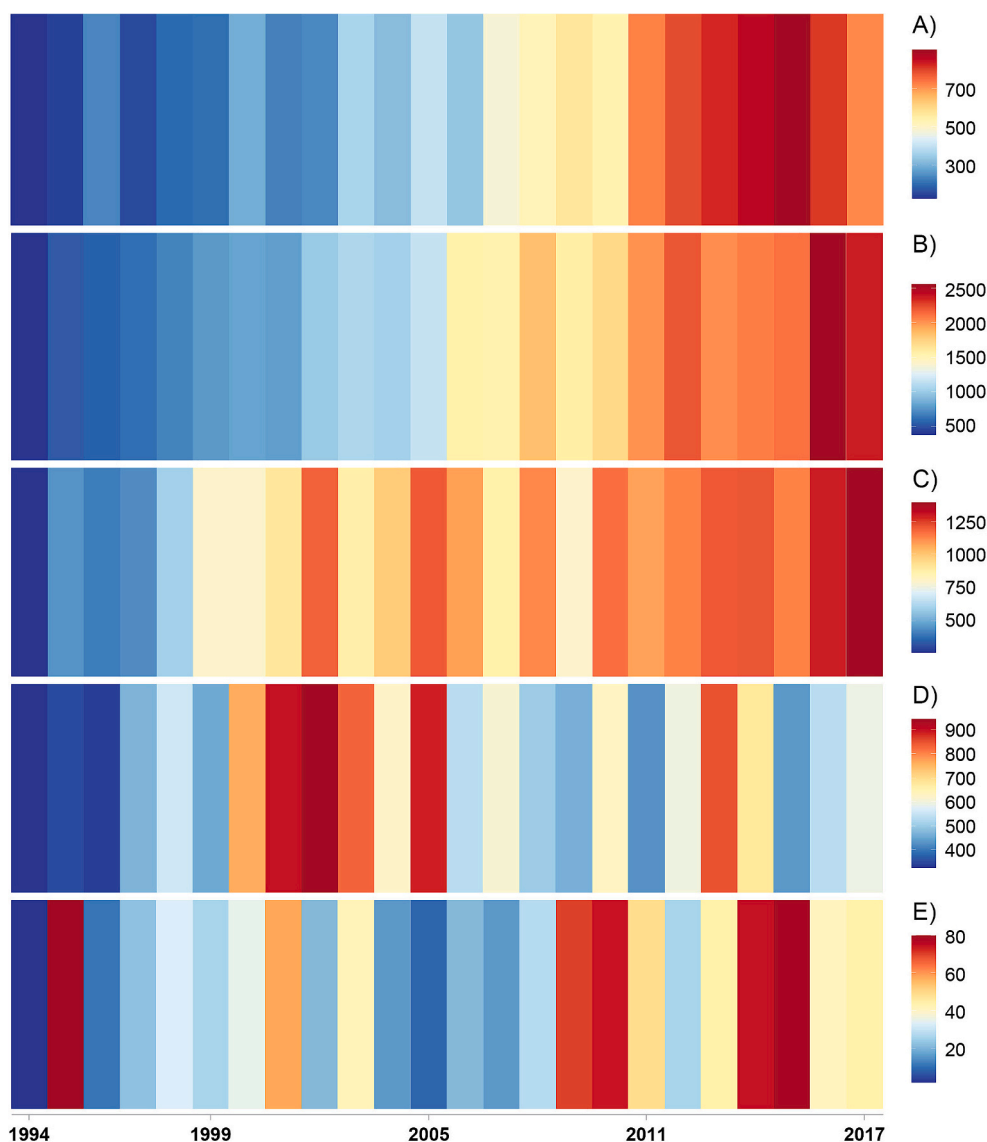


Fig. 5. An overview (stripe plot) of the use information for ethyl palmitate (A), methyl oleate (B), 2,4,7,9-tetramethyl-5-decyn-4,7-diol, TMDD (C), di-*n*-hexyl phthalate, DnHP (D), and hexadecanenitrile (E) during period from 1994 to 2017. The vertical scale depicts number of patents/references.

automated and expanded to include screening of organoiodine compounds. The work also resulted in the discovery of additional contaminants, including a number of CECs, which may be of interest for suspect screening in other samples from the Baltic Sea.

In the course of this work, 254 compounds that exhibited statistically significant temporal trends in Baltic blue mussel and eelpout were tentatively identified. The annual change values obtained in the current work were compared to available data retrieved from scientific literature. Overall, a good agreement was observed between the data generated in the current study and previously published results.

A number of compounds, including four CECs and two unidentified brominated compounds, showed levels considerably higher (two to six orders of magnitude) than the commonly monitored contaminants (CB-153 in EI; BDE-99 in ECNI), which might be taken into consideration for future monitoring and risk assessment.

In addition, almost 400 features with unknown structures also showed statistically significant temporal trends, including 134 organoiodine features. These may be targeted in future studies using complementary soft ionization MS techniques, possibly in combination with two-dimensional chromatographic separation.

With the EU Action Plan to prevent and reduce environmental

pollution, the EU has set itself the ambitious goal of creating a toxic-free environment by 2050 (EC, 2021). This work is mostly in line with the data from target analysis demonstrating that the levels of legacy POPs are, in general, declining in both species from the German Baltic coast. However, there are also several compounds with increasing trends. These include a large number of tentatively identified CECs, as well as compounds with unknown structure, which calls for future identification and risk assessment efforts to put the Zero Pollution Ambition on a sustainable path.

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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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CRedit authorship contribution statement

Andriy Rebryk: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data Curation, Sample and data analysis, Writing – Original Draft, Visualization.

Peter Haglund: Conceptualization, Methodology, Validation, Resources, Data Curation, Writing – Review & Editing, Supervision, Project administration, Funding acquisition.

Jan Koschorreck: Conceptualization, Resources, Writing – Review & Editing.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.scitotenv.2023.166282>.

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