

PAPER

View Article Online
View Journal | View Issue



Cite this: *Environ. Sci.: Processes
Impacts*, 2025, 27, 2507

Do human individuals differ in their potential for lipophilic contaminant biomagnification?[†]

Yuhao Chen,^{ab} Terrence H. Bell,^a Ying Duan Lei^a and Frank Wania^{*ab}

Biomagnification is the process that leads to the chemical potential of organic contaminants in an organism exceeding that in its diet. Despite its obvious importance, studies on biomagnification in humans are rare, in particular those that seek to quantify and characterize interindividual differences in biomagnification potential. Applying a method based on equilibrium sampling and chemical analysis of paired dietary and fecal samples we determined the thermodynamic limit to biomagnification (BMF_{lim}) as well as a feces-based biomagnification factor (BMF_F) for a selection of polychlorinated biphenyls in five human volunteers sharing the same diet over a period of five days. Four younger participants displayed similar BMF_{lim} and BMF_F , while an older participant's BMF_{lim} and BMF_F were higher by factors of up to 5 and 7, respectively. These differences were due to divergent dietary digestion efficiencies, with lipid assimilation efficiency ranging from 93 to 99%. Small sample size prevented us from confirming whether lipid assimilation efficiency is influenced by the participants' gut microbiomes. Fugacities in blood and feces, were highly correlated for each participant, but the relationships were different between participants. Only the younger participants had contaminant fugacities in blood that greatly exceeded those in feces, consistent with a fat flush effect, whereas contaminants were close to chemical equilibrium between blood and feces in the older participant. Differences in biomagnification are likely to contribute to the variability in contaminant levels within a population that is typically observed in biomonitoring.

Received 14th April 2025
Accepted 1st July 2025

DOI: 10.1039/d5em00285k

rsc.li/espi

Environmental significance

Human biomonitoring data often reveal large differences in the concentrations of lipophilic organic contaminants between individuals. Common explanations are differences in external exposure, *e.g.* in dietary intake, and in rates of elimination, *e.g.* because of differences in body fat or metabolic capabilities. Here we reveal evidence of another source of potential variability, namely differences in the extent of gastrointestinal biomagnification. We identify two contributing mechanisms. Large differences in lipid assimilation ability, and differences in the extent, or even the occurrence, of a fat flush effect. Because of the important role of microbes in controlling lipid levels in the gut lumen, this study suggests a potential mechanism for how the gut microbiome could influence the accumulation of, and ultimately health effects caused by, lipophilic contaminants.

Introduction

Human exposure to persistent organic pollutants

Persistent organic pollutants (POPs) are a group of contaminants that share similar physical and chemical properties leading to similar undesirable environmental characteristics, including persistence, bioaccumulation,^{1,2} and the potential for long-range transport.³ Elevated levels of POPs in organisms, including humans, can lead to adverse health effects, such as

respiratory and gastrointestinal disease, endocrine disruption, and cancer.^{4,5} Production and use of many POPs, including the polychlorinated biphenyls (PCBs), have been either restricted or banned by the Stockholm Convention.⁶ Yet, the environmental release of POPs globally has not necessarily been eliminated by these bans and restrictions, due to unintentional released as by-products, from in-used products/equipment or during waste disposal.^{7,8} Accordingly, POPs continue to be health concern.

Consequently, much effort over the past decades has focused on human biomonitoring for POPs and on understanding and quantifying human exposure to POPs. Blood is most frequently used for biomonitoring,^{9,10} but samples that can be obtained less invasively, *e.g.*, milk and feces, are also being explored.^{11–13} Dietary intake is generally the dominant human exposure pathway for POPs.¹⁴ However, dietary contaminant intake does not necessarily correlate directly with contaminant levels in the body, because the latter are also influenced by other factors, *e.g.*,

^aDepartment of Physical and Environmental Sciences, University of Toronto Scarborough, 1265 Military Trail, Toronto, Ontario, M1C 1A4, Canada. E-mail: frank.wania@utoronto.ca

^bDepartment of Chemistry, University of Toronto Scarborough, 1265 Military Trail, Toronto, Ontario, M1C 1A4, Canada

[†] Electronic supplementary information (ESI) available: It includes additional text with experimental details, tables with numerical experimentally obtained and calculated results, as well as figures showing relationships of the obtained results. See DOI: <https://doi.org/10.1039/d5em00285k>



the history of chemical exposure and the rate of chemical elimination.¹⁵

Thermodynamic of biomagnification

Biomagnification is the process causing higher chemical potential of a contaminant in an organism than in its diet.^{1,16,17} To better understand the connection between dietary chemical uptake and the internal exposure obtained by biomonitoring, it is crucial to understand the factors influencing biomagnification. The biomagnification potential of a chemical is generally expressed quantitatively using the biomagnification factor (BMF), which is approximated by the ratio between the lipid-normalized concentration in an organism and in its food.^{16,17} A BMF exceeding 1 indicates a biomagnifying chemical. The traditional way to quantify biomagnification involves determining the contaminant levels in the tissue of laboratory animals, hunted wildlife or in lipid biopsies. While such highly invasive methods can be applied when studying biomagnification in animals, *e.g.*, fish,^{18,19} birds,²⁰ and marine mammals,^{21,22} ethical concerns limit their application to humans. Accordingly, empirical studies quantifying biomagnification in humans²³ are exceedingly rare.

The phenomenon of biomagnification poses a thermodynamic conundrum, in that it seemingly involves the transfer of contaminants from diet to tissues against a thermodynamic gradient.¹⁶ Formulated using physical chemical concepts originally devised by Lewis^{24,25} and later adopted to describe environmental contaminant behaviour by Mackay,²⁶ the fugacity in pressure unit of Pa, or escaping tendency, of a biomagnifying contaminant in the tissues of an organisms f_B exceeds the fugacity in its diet f_D , whereas one would expect transport from phases with high to those with low fugacity.¹⁷ The concept of gastrointestinal biomagnification provides an explanation for this conundrum, by positing that the assimilation of dietary components, and in particular of dietary lipids, during digestion lowers the carrying capacity, or Z -value in units of $\text{mol Pa}^{-1} \text{m}^{-3}$, of the gut content, thereby increasing the fugacity in the digested diet above that in the tissues.^{27,28} The process can be further facilitated by a so-called “fat flush” effect, *i.e.*, rapid absorption of lipids into the gut wall during digestion can lead to a temporary increase in the Z -value of the epithelial cells of the jejunum, thus decreasing the fugacity in those cells and accelerating the transport of contaminants from the gut lumen into the tissues.²⁹ Micelles can also accelerate contaminant transport from the gut to tissues by facilitating transfer through an unstirred water layer.¹⁶

Studying biomagnification non-invasively

The existence of gastrointestinal biomagnification has been demonstrated by measuring a gradual increase in lipid-based concentration of POPs, and therefore in the fugacity, in the gut contents of a fish with increasing extent of digestion.²⁸ While it is not possible to collect the gut content of higher animals at different stages of digestion, it is quite easy to collect the completely digested diet in the form of fecal matter. In fact, due to their non-invasiveness, studies with paired diet and feces

samples have been used to establish fecal excretion as the primary route of POPs elimination,^{30,31} and to determine the net absorption or excretion of POPs in humans.^{19,32} Fecal matter has also been used to investigate thermodynamic aspects of POP biomagnification in humans. In particular, by measuring POPs in the gas phase in equilibrium with feces, Moser and McLachlan have measured equilibrium partitioning ratios of PCBs between air and fecal matter, which can be converted to fecal Z -values Z_F using the saturation vapour pressure.³³ Drouillard and Norstrom similarly measured the Z -values for 1,2,3,4-tetrachlorobenzene in paired dietary and fecal samples of a bird, by quantifying the chemical in the gas phase equilibrated with the samples.³⁴ Moser and McLachlan also determined the fugacity of POPs in human feces f_F by combining air-feces partitioning ratios with measured concentrations in the feces.³⁵ Fecal fugacities f_F exceeding those in blood f_B by as much as 10-fold were seen as evidence of the fat flush effect.

Adopting a method relying on chemical equilibration with silicone-coated vials by Mayer *et al.*,^{36,37} we have shown in our previous work that it is possible to measure fugacities and Z -values of a wide range of PCBs in dietary and fecal samples.^{38–40} We have applied this approach to paired diet and fecal samples of a number of zoo-housed mammals. With knowledge of Z_F , Z_D , f_F and f_D , we could derive several thermodynamic parameters quantifying different aspects of the process of gastrointestinal biomagnification. The Z -values, when combined with the dietary ingestion rate and fecal egestion rate G_D and G_F in units of mL per day, yield the thermodynamic limit to an organism's biomagnification factor (BMF_{lim}):⁴¹

$$\text{BMF}_{\text{lim}} = (G_D/G_F) \times (Z_D/Z_F) \quad (1)$$

The ratio of f_F/f_D we called a feces-based BMF (BMF_F).³⁹ The determination of BMF_{lim} and BMF_F only requires paired dietary and fecal samples, *i.e.* they can be obtained non-invasively. Whereas native contaminant levels need not be known for the BMF_{lim} , since the fugacity capacity can be measured using isotopically labelled chemicals spiked onto those samples,³⁹ the determination of BMF_F requires the ability to quantify native contaminant concentrations in diet and feces because fugacities are calculated from the ratio of concentrations and fugacity capacities.³⁹

Here we apply this method to paired dietary and fecal samples of five human volunteers, who shared the same diet for a period of five days. To ensure the determination of BMF_F was achievable, we used a fish-based diet with relatively high expected levels of biomagnifying contaminants. We used silicone-equilibration to measure Z_F , Z_D , f_F and f_D , and calculated BMF_{lim} and BMF_F for the five participants. Because of the possible role of the gut microbiome in lipid digestion, we also applied 16S RNA gene sequencing to characterize the gut bacterial composition of the volunteers immediately prior to the experiment and again at the end of the five days. We further explored the relationship between fugacities in feces and blood, with a view to assess whether the latter could be estimated non-invasively from the former. Taken together, these experiments allow us to quantify differences in the gastrointestinal



biomagnification process in humans and shed new light on the mechanisms underlying those differences.

Reasons for using PCBs in this study

We selected nine PCBs for this study for a number of reasons: despite long-standing restrictions on their production, PCBs continue to be the biomagnifying contaminants most easily quantified in human dietary, fecal and blood samples. While many other organic contaminants can be reliably quantified in the human diet, they either do not biomagnify⁴² or their biomagnification is due to mechanisms other than gastrointestinal magnification (e.g. charged per- and polyfluorinated alkyl substances^{43,44}). Except for the most volatile PCBs, exposure pathways other than the diet can be safely neglected.¹⁴ Furthermore, reliable equilibrium partitioning ratios between silicone and water are required to interpret the amounts of contaminants quantified during polymer-based equilibrium sampling in term of fugacities and *Z*-values. Such ratios are well-established for many PCB congeners,⁴⁵ are largely unknown for many emerging contaminants, and cannot readily be estimated, e.g. from regressions with the octanol water equilibrium partitioning ratio.⁴⁶ Finally, many of the aspects of gastrointestinal biomagnification discussed here, such as BMF_{lim} , are controlled by the physiology of the biomagnifying organism and not by the properties of the chemical.

Materials and methods

Lab materials

Information about the nine selected PCB congeners and all other chemicals used in the experiment, e.g., polymer, solvents, recovery and injection standards, can be found in Tables S1 and S2 in the ESI.†

Sample preparation and collection

Details of sample preparation and sample collection are given in Text S1 and S2.† The study protocol was reviewed and approved by a Research Ethics Board at the University of Toronto (#43760). Briefly, commode specimen collectors, baked aluminum foil, coolers and glass jars were provided to participants prior to the study period. The volunteers shared the same dietary composition over a five-day period. The diet included but was not limited to fish (e.g., salmon and herring), beef, pork, cheese, rice, pasta, vegetables (e.g., lettuce), fruits (e.g., banana and apple), pork blood, corn and enoki mushrooms. Volunteers collected fecal samples (>1 g) prior to their first meal and all feces produced during the study period. Dietary and fecal samples were wrapped with clean aluminum foils, then transferred into glass jars and stored at $-20\text{ }^{\circ}\text{C}$. Individual dietary intake and fecal egestion were recorded gravimetrically. Around 30 g of blood samples were collected by a family doctor and stored in the collection tubes at $-20\text{ }^{\circ}\text{C}$.

The fecal samples collected by each participant during the study period and the dietary samples were pooled and homogenized using a blender, adding deionised water when necessary to ensure a smooth puree. There were therefore five fecal

sample and one dietary sample. The homogenates were stored in clean glass jars at $-20\text{ }^{\circ}\text{C}$. To spike the dietary and fecal samples, 9 mL of 100 ng mL^{-1} of labeled polychlorinated biphenyls ($^{13}\text{C}_{12}$ -PCBs) (i.e. $^{13}\text{C}_{12}$ -PCB-28, -52, -101, -138, -153 and -180) were pipetted into a baked 1 L amber glass jar rotating horizontally on a roller-mixer at 60 rpm. The jar was allowed to stay on the roller-mixer until the solvent had evaporated completely. Then, around 450 g of sample puree was transferred into the 1 L jar with 4.5 g of sodium azide.

Sample extraction, clean-up and analysis

The detailed extraction and clean-up method and instrumental analysis are described in our previous works^{50,51} and given in Text S3.† Blood, dietary and fecal samples, as well as the associated blank samples, were spiked with 1 ng of five isotopically labelled PCBs (i.e. $^{13}\text{C}_{12}$ -PCB-32, -47, -77, -141 and -188) as internal recovery standards in order to monitor the extraction efficiency. Contaminants were extracted from blood by liquid-liquid extraction using three portions of 100 mL of 1 : 1 hexane : ethyl ether.⁵⁴ Clean-up and volume reduction of blood extracts were exactly the same as those for dietary and fecal samples. Recoveries, given in Table S2,† ranged from 45 to 98%. Recovery during the extraction of blood was relatively low because an emulsion layer prevented a clear separation of solvent and blood during the liquid-liquid extraction. The concentrations of the native and labelled PCB congeners in different samples are given in Tables S3 and S4.†

Equilibrium passive sampling

Preparation of silicone-coated vials and equilibrium passive sampling followed previous works.^{38–40} Five groups of three 40 mL vials each (2 samples + 1 blank) were coated with silicone films of variable thickness (i.e., 4, 6, 8, 10 and 12 μm for diets; 0.2, 0.4, 0.6, 0.8 and 1 μm for fecal matters) for each biological sample, for a total of 90 silicone-coated vials. The PCB concentrations in the silicone were obtained from the slopes of the regression lines between the amount of PCB quantified in the silicone of a vial and the volume of that silicone (Fig. S1 and Table S5†).

Gut microbiome analysis

Details of the gut microbiome analysis were the same as described previously.⁴⁰ Briefly, the DNA were extracted from feces using a Qiagen PowerSoil® DNA Extraction Kit following the manufacturer's instructions and then sent to Genome Quebec (Montreal, Quebec), where 16S rRNA gene amplicon libraries were prepared using the V4-targeting 515F/806R primer set⁴⁷ and sequenced on an Illumina NextSeq (PE300). All raw reads were submitted to NCBI and are available under the BioProject ID PRJNA1087346.

Sample size

Being restricted to only five individuals, this study is inevitably limited in the extent to which it can derive conclusions of wider applicability. This small sample size was necessitated by (i) the



logistical challenge posed by the need for study participants from different households to consume identical food for five days, and (ii) the effort involved in reliably quantifying contaminant *Z*-values and fugacities (*e.g.* each fecal sample required ten separate equilibration experiments). We note that a small sample size is not unusual in this type of work (*e.g.* $n = 1$,^{11,48} $n = 4$,³⁵ $n = 5$,³³ $n = 6$,³¹ $n = 7$ ²⁹).

Results

Dietary digestion efficiency

The five human volunteers, *i.e.*, three males (M) aged 58 (M58), 31 (M31) and 30 (M30) and two females (F) aged 35 (F35) and 24 (F24), shared the same fish-based diet (*e.g.*, herring, tuna, salmon) (Table S6†). M31 and F24 had the highest body-mass normalized G_D and G_F around 20 and 4 mL per day per kg (on a wet weight basis) respectively (Fig. 1). The other volunteers consumed similar amounts of foods (around 16 mL per day per kg) but produced ~50% less feces (about 2 mL per day per kg) than M31 and F24. Even though they shared a diet with the same composition, the five volunteers therefore differed widely in their digestion efficiency. The G_D/G_F ratio averaged 7.4 and ranged from ~5.7 for M31 and F24 to 8.9 for M30 and F35, *i.e.*,

showed deviations as high as almost 50%. In other words, M30 and F35 had the highest digestion efficiency (DE%) of 89%; while M31 and F24 only had a DE% of 82%. The DE% did not correlate with age ($R^2 = 0.1$; Fig. S2b†) but may be related to interindividual differences in water absorption efficiency and gut microbial activity, which determine the fecal water (~90% in wet weight, w.w.) and organic matter (up to 54% in dry weight, d.w.) content, respectively.⁴⁹ A water absorption efficiency could not be calculated in this study since the volumes of water consumed or shed was not recorded. However, we found the water content of 86% in M58's feces, was lower than that in the feces from the four younger participants, which was 92% on average.

Lipid assimilation efficiency

The shared diet had a relatively high lipid content of ~7% in w.w. While the feces of M58 only had 0.65% lipids in w.w., none of the younger participants reduced the lipid content in their feces below 1.9%. The lipid assimilation efficiency (AE_{lipids}) of the five volunteers during the study period (Table S7†) averaged 96%. M30 and F35 had a relatively high lipid assimilation efficiency of 96%, followed by F24 (95%) and then M31 (93%). The

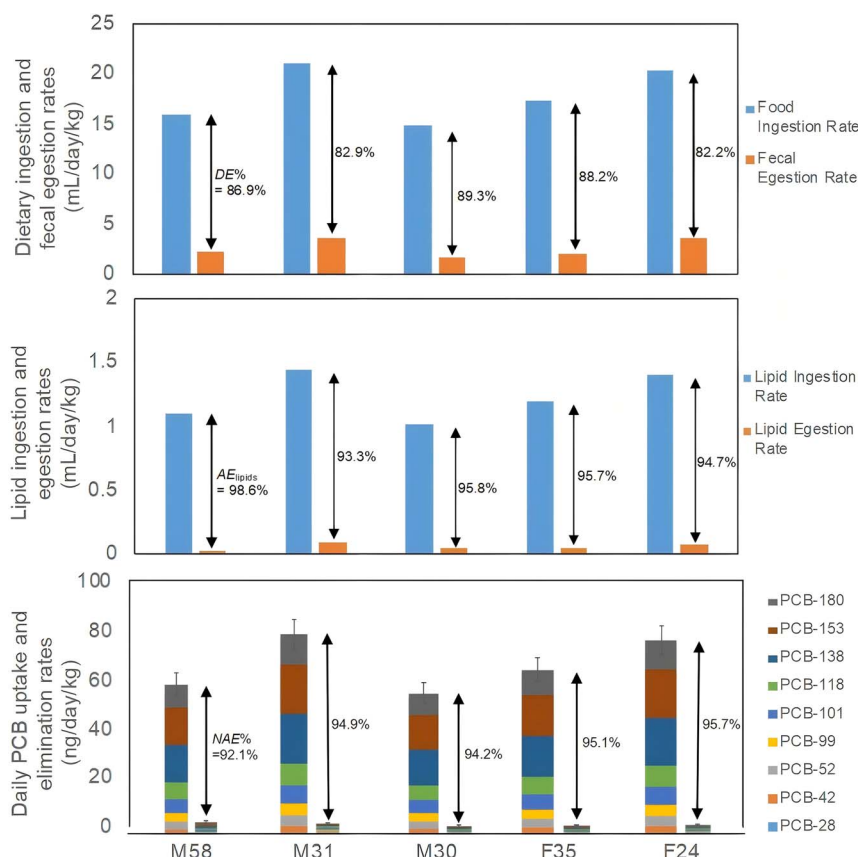


Fig. 1 Dietary ingestion and fecal egestion rates (in units of mL per day per kg), lipid ingestion and egestion rates (in units of mL per day per kg) and daily PCB uptake and elimination rates (in units of ng per day per kg) for five volunteers. Digestion efficiencies (DE%), lipid assimilation efficiencies (AE_{lipids}) and net absorption efficiencies of Σ PCBs (NAE%) are also shown. No standard deviation in the upper panels is provided, because the data were obtained for the entire five days of the experimental period and do not represent the average of multiple daily measurements. The error bars in the lower panel display the standard deviation of triplicate analyses for the sum of the 9 PCB congeners.



oldest volunteer (M58) had the highest AE_{lipids} of 99% (Table S7†). As a result, AE_{lipids} increased with age ($R^2 = 0.7$, Fig. S2a†). Animal studies suggest that the absorbability of lipids increases with age due to changes in thickness and/or character of the unstirred water layer overlying the epithelial cell membrane.⁵⁰

Dietary PCB intake

The sum of the concentrations of 9 selected PCB congeners (*i.e.*, PCB-28, -44, -52, -99, -101, -118, -138, -153 and -180) in the diet was 4.0 ng mL^{-1} and was dominated by the congeners 138 and 153 (Table S7†). The total dietary PCB intake rate of the volunteers during the study period averaged 71 ng per kg per day (Fig. 1) and ranged from 58 (for M30) to 83 ng per kg per day (for M31). This is much larger than is estimated for typical Canadians (ranging from 4 to 8 ng per kg per day),⁵¹ which can be explained by the diet having an unusually high animal lipid content.

Fecal PCB egestion

The sum of the concentrations of the 9 selected PCB congeners in feces was 1.7 ng L^{-1} and thus around 2 times lower than the dietary levels (Table S3†). The fecal egestion rate for the five participants averaged 3.9 ng per kg per day. M58 had the highest PCB elimination rate of 5.0 ng per kg per day, followed by M31 (4.2 ng per kg per day) and the other three volunteers ($\sim 3.4 \text{ ng per kg per day}$). The fecal PCB excretion rates and the dietary PCB intake rates were not correlated ($R^2 = 3 \times 10^{-4}$; Fig. S3†).

Net PCB absorption

By analysing the paired diet and feces, we could determine the net absorption (as the percentage of intake) of the PCBs. All volunteers had a very high net absorption efficiency of the selected PCB congeners, averaging for the sum of nine congeners at 92.4% and ranging from a low of 91.2% for M58 to 93.5% for F24. The net absorption efficiencies varied between the PCB congeners (ANOVA analysis, $p < 0.05$), with generally lower values of 86% for less chlorinated congeners, *e.g.*, PCB-44 and -52 and higher values of up to 97% for highly chlorinated congeners, *e.g.*, PCB-180 (Fig. S4†). Though having few chlorines, PCB-28 had a high net absorption efficiency of 95%. The net absorption of a wide range of POPs, including PCBs, polychlorinated dibenzo-*p*-dioxins-furans, and hexachlorobenzene, has previously been reported as differing widely, ranging from negative values, indicating net excretion, to 100%, indicating complete absorption.^{29,30,33,48,52} Net excretion was associated with a high POP body burden, either because of accidental exposure⁵³ or because older individuals had experienced higher exposure in the past.^{29,32} Very high net absorption was associated with high dietary intake rates, *e.g.* in a newborn infant.⁵⁴ During a high intake experiment all participants had a net absorption of PCB-153 well above 80%, only to experience net excretion when switching to a diet with low contaminant levels.³³ The high PCB net absorption efficiencies above 90% measured here are therefore consistent with the high dietary uptake rate. The slightly lower net absorption in the older

participant (M58) may be related to higher PCB exposure experienced in the past.

Biomagnification limit BMF_{lim}

The BMF_{lim} is referred to as the thermodynamic limit to an organism's biomagnification capability. It quantifies the extent to which an organism's digestive system reduces the capacity of the diet to retain lipophilic contaminants, by reducing both the diet's volume and *Z*-value. The BMF_{lim} thus expresses an individual organism's biomagnification capability. The BMF_{lim} for six PCB congeners determined for the five volunteers in this study are given in Table S8† and displayed in Fig. 2. No BMF_{lim} of PCB-42, -99 and -118 are reported since the *Z*-value of PCBs were determined using isotope-labelled standards and the standards of those three PCBs were not available. M58 had the highest BMF_{lim} ranging from 56 (for PCB-28) to 116 (for PCB-138). The BMF_{lim} in M30 and F35 were almost identical and ranged from 14 (for PCB-28) to 34 (for PCB-153). M31 and F24 had the lowest BMF_{lim} , up to 27 (for PCB-153).

In our earlier work with mammals, the BMF_{lim} was not compound-specific, but rather related to the dietary lipid content, and the physiological condition of the digesting organisms (digestion efficiency and AE_{lipids}).^{38–40} In this study, the BMF_{lim} neither varies strongly between congeners (Table S8†). The BMF_{lim} for PCB-153 is at most a factor of 2.5 higher than the BMF_{lim} of PCB-28 in the same participant. Because lipids contribute most to the *Z*-value of diet and feces, *i.e.*, 58% and 65% on average, respectively (Table S12†), differences in the Z_D/Z_F ratio, and therefore in BMF_{lim} , are closely related to the ratio of the lipid content in food and feces, which is not compound-specific.

The difference in the BMF_{lim} between volunteers was up to a factor of 5.5. Since all volunteers shared the same food and the dietary fugacity capacities Z_D remained the same, the BMF_{lim} values were only influenced by the G_D/G_F ratio and the fecal fugacity capacities Z_F (given for different PCBs in Table S9 and Fig. S5†). Consistent with the low fecal lipid content, the Z_F in M58's feces were the lowest among the five volunteers, ranging from $1 \times 10^3 \text{ mol Pa}^{-1} \text{ m}^{-3}$ for PCB-28 to $1 \times 10^5 \text{ mol Pa}^{-1} \text{ m}^{-3}$ for PCB-180. The Z_F for other participants were 4 to 5 times higher, which means differences in Z_F between the participants explain most of the variability in BMF_{lim} , whereas differences in the digestion efficiency G_D/G_F contribute less, but non-negligibly to the differences in BMF_{lim} .

Feces-based biomagnification factor BMF_F

The BMF_F was obtained as the ratio of the measured fugacities in diet and feces. M58 had the highest BMF_F s, ranging from 3 to 9, followed by F35 and M30, who had BMF_F s ranging from 0.4 to 3, and then M31 and F24, whose BMF_F s ranged from 0.1 to 2 (Table S8†). Some of the BMF_F , *e.g.*, for PCB-28 and -180 in the four younger participants, were below 1, indicating absence of gastrointestinal biomagnification. The BMF_F in the five volunteers share the same congeneric pattern, *i.e.*, peaking at PCB-52 and -101, and reaching a minimum for PCB-28 (Fig. 2).



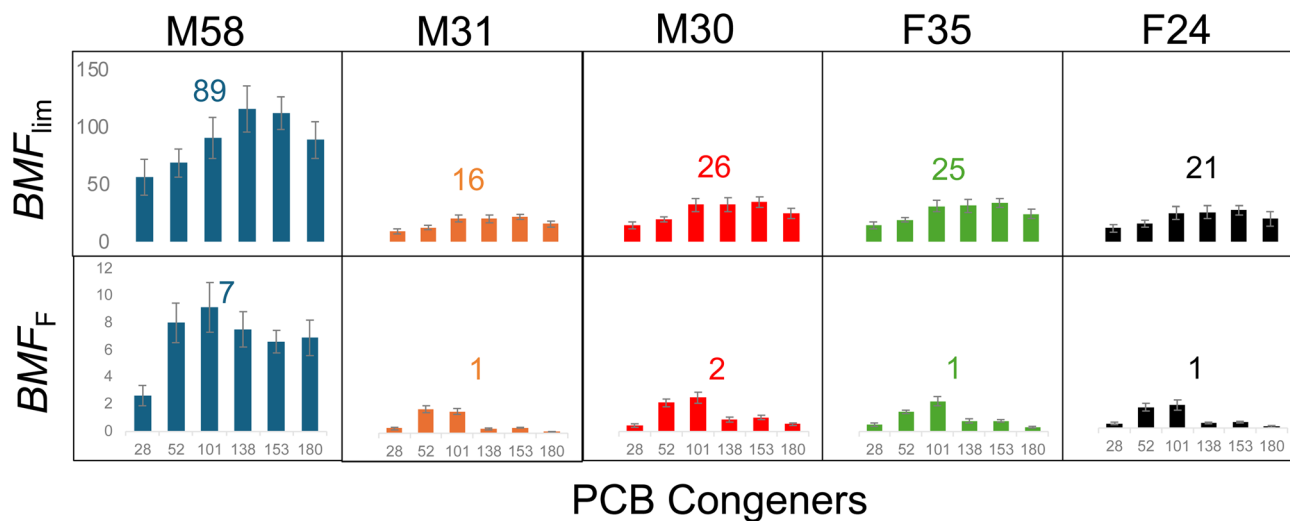


Fig. 2 Thermodynamic biomagnification limits (BMF_{lim}), feces-based biomagnification factors (BMF_F) for the five study participants. The numerical values represent the average biomagnification parameter for 6 congeners.

The BMF_F shows larger differences between congeners than BMF_{lim} , because f_F is to some extent influenced by the body burden, which is dependent on the history of PCB uptake and the rate of elimination. The elimination rate is congener specific because the rate of biotransformation can vary considerably between congeners,⁵⁵ which can explain the congener dependence of BMF_{lim} . The highest BMF_F , observed for either PCB-52 or PCB-101 is on average 10 times higher than the lowest BMF_F , observed for PCB-28 or PCB-180 (Table S8† and Fig. 2). This congeneric pattern for the BMF_F in humans is very similar to that observed for zoo-housed polar bears.⁴⁰

Comparing BMF_{lim} and BMF_F

When averaged across six congeners, the BMF_{lim} , ranging from 16 to 89 for different individuals, is higher than the BMF_F , ranging from 1 to 7. This not only true for the averages, but also applies to each investigated PCB congener and each individual. BMF_{lim} being higher than the BMF_F is consistent with the interpretation of BMF_{lim} as the upper thermodynamic limit to an organism's biomagnification capability.⁴¹ BMF_{lim} and BMF_F are strongly correlated for all congeners and for the average across congeners (Fig. S10A†). Both parameters are proportional to, and therefore strongly influenced by the variability in, the Z_D/Z_F ratio. Because Z_D/Z_F is multiplied with G_D/G_F (~ 7) to obtain BMF_{lim} and with C_F/C_D (~ 0.5) to obtain BMF_F , the former has much higher numerical values than the latter. Using the same set of BMF data but regressing them for different participants, the correlations between the BMF_{lim} and BMF_F were weak (Fig. S10B†). This is because BMF_F are congener-specific, but BMF_{lim} is not.

PCB concentrations in blood

Concentrations of the sum of nine selected PCB congeners in blood varied little between the four participants, ranging from 0.4 ng mL^{-1} for F24 to 0.7 ng mL^{-1} for F35 (Table S4†). No blood

was sampled from M31. As the lipid content in blood ranged from 1 mg mL^{-1} to 2 mg mL^{-1} , this translates to lipid-normalized concentrations between $238 \text{ ng per g lipid}$ for F24 and $411 \text{ ng per g lipid}$ for F35 (Tables S4 and S6†), which is above the range of PCBs serum levels reported for Canadians in the Canadian Health Measures Survey.⁹ Whereas the relative PCB composition was very similar between the three younger volunteers, the three heavier PCBs 138, 153 and 180 were relatively much more abundant in M58's blood (55% of the sum of nine congeners vs. 31% on average for F24, M30 and F35) (Fig. S6†). In fact, the percentage contribution of these three congeners had a very strong linear relationship with age (Fig. S7†). This is consistent with the much longer residence time of these highly chlorinated congeners in the human body, implying that the body retains a "memory" of past exposure to these congeners for a longer period.⁵⁶

Fugacities of PCBs in blood

We estimated the fugacities of PCBs in human blood f_B by using the measured lipid-normalized concentrations (Table S10†) and Z -values for storage lipids estimated for the PCBs (Table S11†) using the equilibrium partitioning ratio between storage lipids and water ($K_{\text{storage-lipid/w}}$)⁵⁷ and the Henry's law constant.⁵⁸ This calculation assumes that lipids are solely responsible for sorbing PCBs in blood and that the blood lipids have the partitioning properties of generic storage lipids. For most participants, fugacities in blood were higher than in feces, whereas in M58 fugacities in blood and feces were very similar.

It may be tempting to estimate an actual biomagnification factor from the ratio of the fugacities in blood and diet f_B/f_D . However, a BMF applies to a steady-state situation when contaminant uptake and elimination are equal, *i.e.*, if there is no net uptake.^{16,17} The unusually high dietary PCB concentration during the experiment (*i.e.* a high f_D) means that the ratio f_B/f_D is unlikely to capture a steady state situation and would be



biased low. The observed high net absorption efficiencies for the PCBs indeed indicate a situation far from steady state.

Gut bacterial composition

Bacterial biomass accounts for as much as half of the organic matter in human feces.⁴⁹ The abundance of certain gut microbes may influence lipid assimilation efficiency, and therefore the biomagnification capability of an organism,^{59,60} while antibiotics can reduce lipid absorption by lowering the intestinal permeability of lipids.⁶¹ To investigate the relationship between the gut microbiome and biomagnification, we assessed the bacterial composition of feces using high-throughput 16S rRNA gene amplicon sequencing. Because gut microbial composition can shift rapidly with a change in diet,^{59,62–64} this was done using feces collected immediately prior to the experiment and again at the end of the study period.

Bacterial composition remained very consistent for M58 and M31, while F24, F35 and M30 experienced a shift in their gut microbial composition during the experimental period (Fig. S8†). For example, the relative abundance of Bacteroidales was reduced significantly after switching from a meat- to a fish-based diet, but Lachnospirales dominated in F24's gut microbiome. Both M30 and F35 experienced a drop of relative abundance of Oscillospirales, and an increase in that of Bacteroidales. The relative abundance of Lachnospirales also decreased in F35 but remained unchanged in M30 even though they share a regular diet. The composition of the gut microbiomes saw significant changes for F24 but not for M31 when switching from a non-fish-based diet (*e.g.*, cheese, beef, pork, chicken, milk) to a fish-based diet. When bacterial taxa were grouped at genus, order, and phylum levels, F24 was an outlier in all cases, clustering most closely with a set of canine samples reported in our previous work (Fig. S9†).⁴⁰

Discussion

Can we estimate BMF_{lim} from $\text{AE}_{\text{lipids}}$?

In Fig. 3 we plot all BMF_{lim} values we have determined for various organisms (average of PCB congeners 28, 52, 101, 138, 153 and 180) against an organism's measured lipid assimilation efficiency $\text{AE}_{\text{lipids}}$.^{38–40} The $\text{AE}_{\text{lipids}}$ for the human participants are generally lower than those of the dog, Arctic wolves and polar bears, but the data point for M58 aligns well with those for the animals, suggesting the existence of a generally applicable relationship. If the Z-value of diet and feces is solely determined by their lipid content, we can derive the following simple relationship between BMF_{lim} and $\text{AE}_{\text{lipids}}$ (see Text S4† for detail):

$$\text{BMF}_{\text{lim}} = 1/(1 - \text{AE}_{\text{lipids}}) \quad (2)$$

which is represented by the line in Fig. 3. The agreement between the measured BMF_{lim} and the one calculated from eqn (2) is remarkable and suggests that BMF_{lim} can be predicted from $\text{AE}_{\text{lipids}}$ with high confidence. $\text{AE}_{\text{lipids}}$ is easy to measure, requiring only the dietary and fecal lipid content. In contrast, no clear relationship is apparent between the BMF_{F} , averaged across congeners, and $\text{AE}_{\text{lipids}}$ (Fig. S11†).

Can we estimate the fugacity in blood f_{B} from the fugacity in feces f_{F} ?

Whereas fugacities in paired feces and blood samples have not previously been measured or correlated, Schlummer *et al.*²⁹ and Chen *et al.*¹² have reported correlations between the concentration of PCBs in human feces and in human blood. The slope of these relationship, interpreted as feces : blood partitioning ratios, was found to be influenced by the physiological development of the human gastrointestinal system during the first year of their life¹¹ and by the digestion efficiency³³ and the

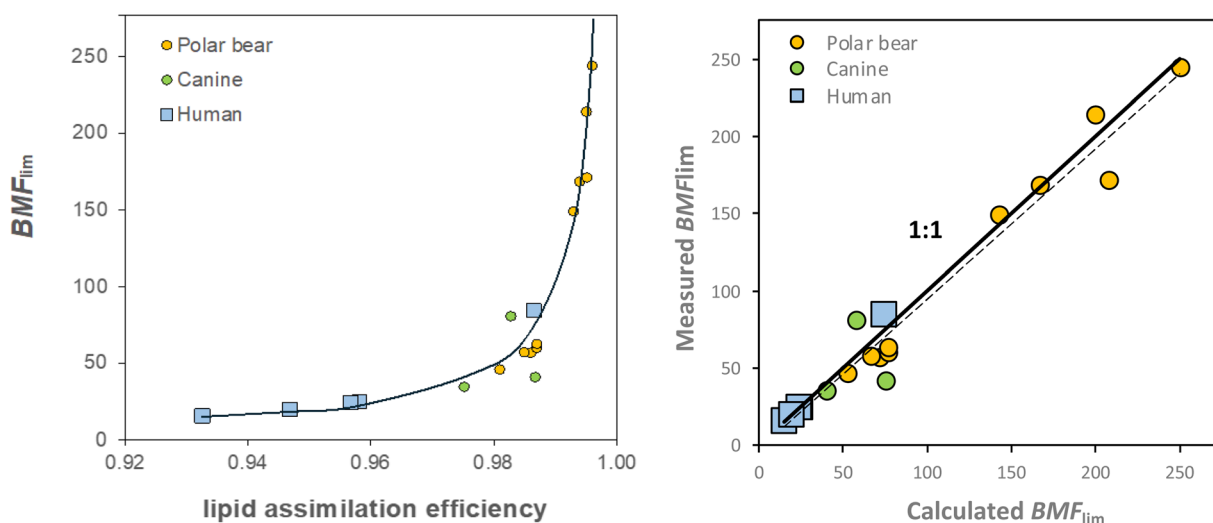


Fig. 3 Relationship between the thermodynamic biomagnification limit measured for polar bears, canines (dog and Arctic wolves) and humans and their lipid assimilation efficiency (left); the solid line is not a fit, but the theoretical relationship described by eqn (2), which assumes that the dietary and fecal Z-values are solely determined by lipid content. The relationship between the measured BMF_{lim} and the BMF_{lim} calculated using eqn (2) (right).



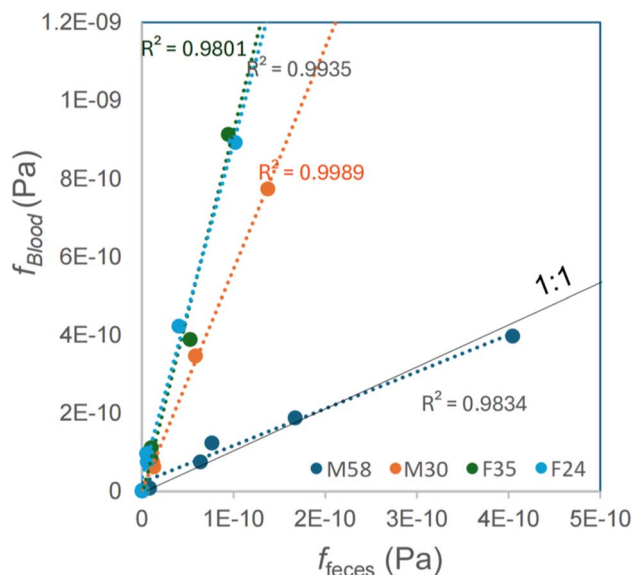


Fig. 4 Relationship between the fugacity of PCBs in feces and blood for different volunteers. Data of PCB-28 are not included in the graph.

dietary composition.¹² In our study, the correlation between the f_F and f_B is very strong for all four participants ($R^2 > 0.98$) (Fig. 4). PCB-28 was removed from this correlation analysis, because its concentrations in blood are only marginally above the method detection limit (Table S13†) and – when combined with the estimated fugacity capacity of blood – yield very uncertain f_B . Despite the strong correlation of f_F and f_B for an individual, the slopes of their relationships deviate between individuals (Fig. 4). Specifically, while the relationships are essentially identical in M24 and F35, the slope for M58 is much lower (Fig. 4). In other words, while there appears to be an opportunity to estimate f_B from f_F and therefore derive BMF non-invasively, this would require “calibrating” individual-specific relationships first, which is not practical.

Inter-individual differences in biomagnification

Overall, the biomagnification behaviour of the younger participants is strikingly similar, but remarkably different from that of M58. On the one hand M58 has consistently higher BMF_{lim} and BMF_F than the other study participants (Fig. 2). On the other hand, feces and blood of M58 are close to equilibrium with respect to PCBs, whereas f_B was clearly larger than f_F for the younger participants (Fig. 4). Whereas the previously observed “fat flush” effect^{29,35} was thus evident in the younger participants, it is largely absent in M58.

The differences in BMF_{lim} and BMF_F are statistically significant: when averaged across PCBs, BMF_{lim} and BMF_F are very similar in the younger participants (one-way ANOVA test, $p > 0.05$), but up to 5.5- and 7-fold higher, respectively, in M58 (one-way ANOVA test, $p < 0.05$). The explanation is the very low fecal lipid content in M58 indicative of a high very AE_{lipids} more in line with that of the zoo-housed animals (Fig. 3). Incidentally, BMF_{lim} and BMF_F also show the same congeneric dependence

in the younger participants (Fig. 2), while the BMF_F for PCB-138, -153 and -180 is relatively higher in M58, because of a higher body burden of those three congeners (Table S4† and Fig. S6†), which led to a net absorption efficiency of 93%, lower than the 97% of the younger participants.

Fugacities in blood that exceed those in feces as we observe for the younger participants is consistent with the “fat flush” effect that has previously been observed to cause f_B to exceed the f_F 10-fold.^{29,35} While we cannot be sure about the reasons why no fat flush is apparent in M58, we put forward two potential explanations, one related to changes in the lipid content of the gut lumen after equilibration in the jejunum, the other related to potentially reduced peristalsis in M58.

Lipophilic chemicals diffuse most effectively across the gut epithelium, *i.e.* are taken up in the upper part of the small intestine, whereas excretion occurs from the large intestine.⁶⁵ When the digested food passes through the gastrointestinal tract, its composition will be changed by epithelial cells being sloughed off from the gut wall and the bacteria growing in the large intestine, *e.g.*, the lipid content of the gut content may increase again in the large intestine, since 40% of lipids in the feces originates from bacterial activities.²⁹ Therefore, the fugacity capacity in lumen may increase when passing through the large intestine, thus decreasing the fugacity in lumen. We hypothesize that blood and lumen equilibrate in the small intestine and have similar contaminant fugacities. The lipid content of lumen is at a minimum here because of the ready assimilation of dietary lipids in the small intestine. In the gastrointestinal tract of the four younger participants, the lipid content of the lumen may increase again in the large intestine, *e.g.* because of bacterial growth. This lowers the fugacity in the lumen/feces relative to that in the blood. In M58, however, the lipid content of the lumen may not increase in the large intestine (possibly because of a specific gut microbiome). This would explain the low fecal lipid content and the similarity of the fugacity in feces and blood.

While M58 depleted the dietary lipid content to extremely low levels, this lipid absorption may have occurred over a longer period than in the younger participants. Whereas aging has little influence on lipid digestion and absorption in a healthy human,⁶⁶ intestinal peristalsis can decrease with aging resulting in a longer retention time of food in the gut.⁶⁷ Some corn kernels consumed on day one were present in M58's feces on day three, whereas younger participants excreted all corn within one (M31, F35, F24) or two days (M30), which may indicate slower intestinal peristalsis in M58. A longer residence time of foods may result in lipid absorption being spread out over a longer period, suppressing the “fat flush” effect. Other age-related factors, *e.g.*, the decreases in the intestinal surface area⁶⁸ may also influence the “fat flush” effect.

Incidentally, while the very high AE_{lipids} increases the biomagnification potential of M58, the absence of a fat flush reduces it. The overall cancellation of the two effects is apparent in blood fugacities for the PCBs that are similar between M58 and the younger participants (Table S10†).



Implications

Human biomonitoring for PCBs and other POPs reveals large differences in blood concentrations⁷⁰ even for individuals within the same age cohort.^{9,52,69,71} For example, the concentration of PCB-138 in the serum of Canadians in their 40s and 50s has been reported to range from 0.02 to 25 ng per g lipids, *i.e.*, over three orders of magnitude.⁹ These differences are largely assumed to be a result of differences in external exposure, most notably differences in dietary intake, between individuals.⁷² Other factors that could contribute to such differences include interindividual differences in rates of elimination,^{73,74} as influenced by differences in body fat¹⁵ or metabolic capabilities.^{75,76} However, modelling shows that these factors cannot fully explain the observed variability.⁷⁷

Here, we show that differences in the biomagnification capacity of different individuals may also contribute to the variability observed in human biomonitoring. In particular, large differences in lipid assimilation efficiency and in the extent of a “fat flush” effect between individuals could influence how much of the POPs ingested with the diet is taken up in the body. While it can be hypothesized that lipid assimilation efficiency and the extent of a “fat flush” effect is determined by the gut microbiome, we could not show a significant relationship between the gut microbial composition and BMF_{lim} through a redundancy analysis when only humans were included in the model (data not shown). This may be due to the combination of a small sample size and gut microbiomes that were very different between the participants. While the interindividual differences reported here are admittedly based on a very small sample number, we note that earlier studies with zoo-housed polar bears not only revealed similarly large interindividual differences in biomagnification, but also indicated more clearly the role of the gut microbiome.⁴⁰

Studies with much larger numbers of participants would be required to establish the extent of interindividual differences in human biomagnification more broadly and to tease out the role of any possible relationship between the gut microbiome and lipid assimilation efficiency. Future studies should include a wide range of ages to confirm whether the remarkable divergence between M58 and the other study participants is due to age. Furthermore, with a larger sample size the factors influencing the relationship between f_B and f_F may be established, possibly paving the way to estimate also the f_B non-invasively.

Data availability

All data generated in this project are contained in the ESI file.†

Conflicts of interest

The authors declare no competing financial interest.

Acknowledgements

We acknowledge funding from a Discovery Grant of the Natural Sciences and Engineering Research Council of Canada (grant

number: RGPIN-2020-04142; F. W.). We thank all study participants, not least for preparing the delicious food for each other. We are grateful to Calvin Lei for blood sampling and to Michael McLachlan for a thorough critique of this manuscript.

References

- 1 B. C. Kelly, M. G. Ikonou, J. D. Blair, A. E. Morin and F. A. P. C. Gobas, Food web-specific biomagnification of persistent organic pollutants, *Science*, 2007, **317**(5835), 236–239, DOI: [10.1126/science.1138275](https://doi.org/10.1126/science.1138275).
- 2 G. Czub and M. S. McLachlan, Bioaccumulation potential of persistent organic chemicals in humans, *Environ. Sci. Technol.*, 2004, **38**(8), 2406–2412, DOI: [10.1021/es034871v](https://doi.org/10.1021/es034871v).
- 3 M. Scheringer, Long-range transport of organic chemicals in the environment, *Environ. Toxicol. Chem.*, 2009, **28**, 677–690, DOI: [10.1897/08-324R.1](https://doi.org/10.1897/08-324R.1).
- 4 D. Orlinskii, I. Priputina, A. Popova, A. Shalanda, T. Tsongas, G. Hinman and W. Butcher, Influence of environmental contamination with PCBs on human health, *Environ. Geochem. Health*, 2001, **23**(4), 313–328, DOI: [10.1023/A:1012299231348](https://doi.org/10.1023/A:1012299231348).
- 5 A. Brouwer, M. P. Longnecker, L. S. Birnbaum, J. Coglian, P. Kostyniak, J. Moore, S. Schantz and G. Winneke, Characterization of potential endocrine-related health effects at low-dose levels of exposure to PCBs, *Environ. Health Perspect.*, 1999, **107**, 639–649, DOI: [10.1289/ehp.99107s4639](https://doi.org/10.1289/ehp.99107s4639).
- 6 *Stockholm Convention on Persistent Organic Pollutants (POPs)*, access date, April 2024, <https://chm.pops.int>.
- 7 L. Li, C. Chen, D. Li, K. Breivik, G. Abbasi and Y.-F. Li, What do we know about the production and release of persistent organic pollutants in the global environment?, *Environ. Sci. Adv.*, 2023, **2**, 55–68, DOI: [10.1039/D2VA00145D](https://doi.org/10.1039/D2VA00145D).
- 8 K. Breivik, J. M. Armitage, F. Wania, A. Sweetman and K. C. Jones, Tracking the global distribution of persistent organic pollutants accounting for e-waste exports to developing regions, *Environ. Sci. Technol.*, 2016, **50**, 798–805, DOI: [10.1021/acs.est.5b04226](https://doi.org/10.1021/acs.est.5b04226).
- 9 D. F. K. Rawn, J. J. Ryan, A. R. Sadler, W.-F. Sun, D. Haines, K. Macey and J. Van Oostdam, PCDD/F and PCB concentrations in sera from the Canadian Health Measures Survey (CHMS) from 2007 to 2009, *Environ. Int.*, 2012, **47**, 48–55, DOI: [10.1016/j.envint.2012.05.008](https://doi.org/10.1016/j.envint.2012.05.008).
- 10 C. D. Sandau, Analysis of hydroxylated metabolites of PCBs (OH-PCBs) and other chlorinated phenolic compounds in whole blood from Canadian Inuit, *Environ. Health Perspect.*, 2000, **108**(7), 611–616, DOI: [10.1289/ehp.00108611](https://doi.org/10.1289/ehp.00108611).
- 11 Y. Chen, M. S. McLachlan, S. Kaserzon, X. Wang, L. Weijs, M. Gallen, L.-M. Toms, Y. Li, L. L. Aylward, P. D. Sly and J. F. Mueller, Monthly variation in faeces: blood concentration ratio of persistent organic pollutants over the first year of life: a case study of one infant, *Environ. Res.*, 2016, **147**, 259–268, DOI: [10.1016/j.envres.2016.02.017](https://doi.org/10.1016/j.envres.2016.02.017).
- 12 Y. Chen, A. Sjödin, M. S. McLachlan, K. English, L. L. Aylward, J. Varghese, P. D. Sly and J. F. Mueller, Persistent organic pollutants in infants and toddlers:



- Relationship between concentrations in matched plasma and faecal samples, *Environ. Int.*, 2017, **107**, 82–88, DOI: [10.1016/j.envint.2017.06.019](#).
- 13 H. R. Johansen, C. Thorstensen, T. Greibrokk and G. Becher, On-line SFE-GC for determination of PCBs in human milk and blood serum, *J. High Resolut. Chromatogr.*, 1993, **16**(3), 148–152, DOI: [10.1002/jhrc.1240160303](#).
 - 14 L. Li, J. A. Arnot and F. Wania, Revisiting the contributions of far- and near-field routes to human aggregate exposure to polychlorinated biphenyls (PCBs), *Environ. Sci. Technol.*, 2018, **52**, 6974–6984, DOI: [10.1021/acs.est.8b00151](#).
 - 15 M. S. Wolff, H. A. Anderson, J. A. Britton and N. Rothman, Pharmacokinetic variability and modern epidemiology - the example of dichlorodiphenyltrichloroethane, body mass index, and birth cohort, *Cancer Epidemiol. Biomarkers Prev.*, 2007, **16**, 1925–1930, DOI: [10.1158/1055-9965.EPI-07-0394](#).
 - 16 B. C. Kelly, F. A. P. C. Gobas and M. S. McLachlan, Intestinal absorption and biomagnification of organic contaminants in fish, wildlife, and humans, *Environ. Toxicol. Chem.*, 2004, **23**(10), 2324–2336, DOI: [10.1897/03-545](#).
 - 17 D. Mackay, A. K. D. Celsie, D. E. Powell and J. M. Parnis, Bioconcentration, bioaccumulation, biomagnification and trophic magnification: a modelling perspective, *Environ. Sci.: Processes Impacts*, 2018, **20**, 72–85, DOI: [10.1039/C7EM00485K](#).
 - 18 F. A. P. C. Gobas, X. Zhang and R. Wells, Gastrointestinal magnification: the mechanism of biomagnification and food chain accumulation of organic chemicals, *Environ. Sci. Technol.*, 1993, **27**(13), 2855–2863, DOI: [10.1021/es00049a028](#).
 - 19 L. Tao, Y. Zhang, J.-P. Wu, S.-K. Wu, Y. Liu, Y.-H. Zeng, X.-J. Luo and B.-X. Mai, Biomagnification of PBDEs and alternative brominated flame retardants in a predatory fish: Using fatty acid signature as a primer, *Environ. Int.*, 2019, **127**, 226–232, DOI: [10.1016/j.envint.2019.03.036](#).
 - 20 K. M. Fremlin, J. E. Elliott, D. J. Green, K. G. Drouillard, T. Harner, A. Eng and F. A. P. C. Gobas, Trophic magnification of legacy persistent organic pollutants in an urban terrestrial food web, *Sci. Total Environ.*, 2020, **714**, 13674, DOI: [10.1016/j.scitotenv.2020.136746](#).
 - 21 E. G. Sørmo, M. P. Salmer, B. M. Jenssen, H. Hop, K. Bæk, K. M. Kovacs, C. Lydersen, S. Falk-Petersen, G. W. Gabrielsen, E. Lie and J. U. Skaare, Biomagnification of polybrominated diphenyl ether and hexabromocyclododecane flame retardants in the polar bear food chain in Svalbard, Norway, *Environ. Toxicol. Chem.*, 2006, **25**(9), 2502–2511, DOI: [10.1897/05-591R.1](#).
 - 22 R. J. Letcher, W. A. Gebbink, C. Sonne, E. W. Born, M. A. McKinney and R. Dietz, Bioaccumulation and biotransformation of brominated and chlorinated contaminants and their metabolites in ringed seals (*Pusa hispida*) and polar bears (*Ursus Maritimus*) from East Greenland, *Environ. Int.*, 2009, **35**(8), 1118–1124, DOI: [10.1016/j.envint.2009.07.006](#).
 - 23 P. A. Cox, S. A. Banack and S. J. Murch, Biomagnification of cyanobacterial neurotoxins and neurodegenerative disease among the Chamorro people of Guam, *Proc. Natl. Acad. Sci. U. S. A.*, 2003, **100**(23), 13380–13383, DOI: [10.1073/pnas.2235808100](#).
 - 24 G. N. Lewis, The law of physico-chemical change, *Proc. Am. Acad. Arts Sci.*, 1901, **37**, 49–69, DOI: [10.2307/20021635](#).
 - 25 G. N. Lewis, Outlines of a new system of thermodynamic chemistry, *Proc. Am. Acad. Arts Sci.*, 1907, **43**, 259–293, DOI: [10.2307/20022322](#).
 - 26 D. Mackay, Finding fugacity feasible, *Environ. Sci. Technol.*, 1979, **13**, 1218–1223, DOI: [10.1021/es60158a003](#).
 - 27 F. A. P. C. Gobas, J. R. McCorquodale and G. D. Haffner, Intestinal absorption and biomagnification of organochlorines, *Environ. Toxicol. Chem.*, 1993, **12**(3), 567–576, DOI: [10.1002/etc.5620120316](#).
 - 28 F. A. P. C. Gobas, J. B. Wilcockson, R. W. Russell and G. D. Haffner, Mechanism of biomagnification in fish under laboratory and field conditions, *Environ. Sci. Technol.*, 1999, **33**(1), 133–141, DOI: [10.1021/es980681m](#).
 - 29 M. Schlummer, G. A. Moser and M. S. McLachlan, Digestive tract absorption of PCDD/Fs, PCBs, and HCB in humans: mass balances and mechanistic considerations, *Toxicol. Appl. Pharmacol.*, 1998, **152**(1), 128–137, DOI: [10.1006/taap.1998.8487](#).
 - 30 N. O. Price, R. W. Young and J. K. Dickinson, Pesticide residues and polychlorinated biphenyl levels in diets, urine, and fecal matter of preadolescent girls, *Proc. Soc. Exp. Biol. Med.*, 1972, **139**(4), 1280–1283, DOI: [10.3181/00379727-139-36347](#).
 - 31 S. Rohde, G. A. Moser, O. Papke and M. S. McLachlan, Clearance of PCDD/Fs via the gastrointestinal tract in occupationally exposed persons, *Chemosphere*, 1999, **38**(14), 3397–3410, DOI: [10.1016/S0045-6535\(98\)00551-7](#).
 - 32 P. Schrey, J. Wittsiepe, P. Mackrodt and F. Selenka, Human fecal PCDD/F-excretion exceeds the dietary intake, *Chemosphere*, 1998, **37**(9–12), 1825–1831, DOI: [10.1016/S0045-6535\(98\)00248-3](#).
 - 33 G. A. Moser and M. S. McLachlan, The influence of dietary concentration on the absorption and excretion of persistent lipophilic organic pollutants in the human intestinal tract, *Chemosphere*, 2001, **45**(2), 201–211, DOI: [10.1016/S0045-6535\(00\)00551-8](#).
 - 34 K. G. Drouillard and R. J. Norstrom, Use of a vial equilibration technique to measure the change in fugacity capacity of avian food and feces samples for 1,2,3,4-tetrachlorobenzene, *Bull. Environ. Contam. Toxicol.*, 2014, **93**(5), 561–566, DOI: [10.1007/s00128-014-1316-4](#).
 - 35 A. Moser and M. S. McLachlan, Partitioning of polychlorinated biphenyls and hexachlorobenzene into human faeces, *Chemosphere*, 2002, **46**(3), 449–457, DOI: [10.1016/S0045-6535\(01\)00100-X](#).
 - 36 P. Mayer, J. Tolls, J. L. M. Hermens and D. Mackay, Equilibrium sampling devices, *Environ. Sci. Technol.*, 2003, **37**(9), 184A–191A, DOI: [10.1021/es032433i](#).
 - 37 F. Reichenberg, F. Smedes, J.-Å. Jönsson and P. Mayer, Determining the chemical activity of hydrophobic organic compounds in soil using polymer coated vials, *Chem. Cent. J.*, 2008, **2**, 8, DOI: [10.1186/1752-153X-2-8](#).



- 38 Y. Chen, Y. D. Lei, J. Wensvoort and F. Wania, Quantifying the biomagnification capability of Arctic Wolf and domestic dog by equilibrium sampling, *Environ. Sci. Technol.*, 2020, **54**(11), 6842–6849, DOI: [10.1021/acs.est.0c00157](https://doi.org/10.1021/acs.est.0c00157).
- 39 Y. Chen, Y. D. Lei, J. Wensvoort, S. Gourlie and F. Wania, Probing the thermodynamics of biomagnification in zoo-housed polar bears by equilibrium sampling of dietary and fecal samples, *Environ. Sci. Technol.*, 2022, **56**(13), 9497–9504, DOI: [10.1021/acs.est.2c00310](https://doi.org/10.1021/acs.est.2c00310).
- 40 Y. Chen, T. H. Bell, S. Gourlie, Y. D. Lei and F. Wania, Contaminant biomagnification in polar bears: interindividual differences, dietary intake rate, and the gut microbiome, *Environ. Sci. Technol.*, 2024, **58**(24), 10504–10514, DOI: [10.1021/acs.est.4c03302](https://doi.org/10.1021/acs.est.4c03302).
- 41 K. G. Drouillard, G. Paterson, J. Liu and G. D. Haffner, Calibration of the gastrointestinal magnification model to predict maximum biomagnification potentials of polychlorinated biphenyls in a bird and fish, *Environ. Sci. Technol.*, 2012, **46**(18), 10279–10286, DOI: [10.1021/es301724h](https://doi.org/10.1021/es301724h).
- 42 L. P. Burkhard, J. A. Arnot, M. R. Embry, K. J. Farley, R. A. Hoke, M. Kitano, H. A. Leslie, G. R. Lotufo, T. F. Parkerton, K. G. Sappington, G. T. Tomy and K. B. Woodburn, Comparing laboratory and field measured bioaccumulation endpoints, *Integrated Environ. Assess. Manag.*, 2011, **8**, 17–31, DOI: [10.1002/ieam.260](https://doi.org/10.1002/ieam.260).
- 43 Y. Lu, R. Guan, N. Zhu, J. Hao, H. Peng, A. He, C. Zhao, Y. Wang and G. Jiang, A critical review on the bioaccumulation, transportation, and elimination of per- and polyfluoroalkyl substances in human beings, *Crit. Rev. Environ. Sci. Technol.*, 2023, **54**, 95–116, DOI: [10.1080/10643389.2023.2223118](https://doi.org/10.1080/10643389.2023.2223118).
- 44 B. Rispens and A. J. Hendriks, Towards process-based modelling and parameterisation of bioaccumulation in humans across PFAS congeners, *Chemosphere*, 2024, **359**, 142253, DOI: [10.1016/j.chemosphere.2024.142253](https://doi.org/10.1016/j.chemosphere.2024.142253).
- 45 D. Gilbert, G. Witt, F. Smedes and P. Mayer, Polymers as reference partitioning phase: Polymer calibration for an analytically operational approach to quantify multimedia phase partitioning, *Anal. Chem.*, 2016, **88**(11), 5818–5826, DOI: [10.1021/acs.analchem.6b00393](https://doi.org/10.1021/acs.analchem.6b00393).
- 46 F. Smedes, Silicone–water partition coefficients determined by cosolvent method for chlorinated pesticides, musks, organo phosphates, phthalates and more, *Chemosphere*, 2018, **210**, 662–671, DOI: [10.1016/j.chemosphere.2018.07.054](https://doi.org/10.1016/j.chemosphere.2018.07.054).
- 47 Mo BIO Laboratories, Inc., *MO BIO's PowerSoil DNA Isolation Kit Handbook*, 2014, accessed 2023-12-01, <https://www.qiagen.com/us/resources/resourcedetail?id=5c00f8e4-c9f5-4544-94fa-653a5b2a6373&lang=en>.
- 48 M. S. McLachlan, Digestive tract absorption of polychlorinated dibenzo-p-dioxins, dibenzofurans, and biphenyls in a nursing infant, *Toxicol. Appl. Pharmacol.*, 1993, **123**(1), 68–72, DOI: [10.1006/taap.1993.1222](https://doi.org/10.1006/taap.1993.1222).
- 49 C. Rose, A. Parker, B. Jefferson and E. Cartmell, The characterization of feces and urine: a review of the literature to inform advanced treatment technology, *Crit. Rev. Environ. Sci. Technol.*, 2015, **45**(17), 1827–1879, DOI: [10.1080/10643389.2014.1000761](https://doi.org/10.1080/10643389.2014.1000761).
- 50 D. Hollander, V. D. Dadufalza and E. G. Sletten, Does essential fatty acid absorption change with aging?, *J. Lipid Res.*, 1984, **25**(2), 129–134, DOI: [10.1016/S0022-2275\(20\)37833-0](https://doi.org/10.1016/S0022-2275(20)37833-0).
- 51 W. H. Newsome, D. J. Davies and W. F. Sun, Residues of polychlorinated biphenyls (PCB) in fatty foods of the Canadian diet, *Food Addit. Contam.*, 1998, **15**(1), 19–29, DOI: [10.1080/02652039809374596](https://doi.org/10.1080/02652039809374596).
- 52 C.-Y. Juan, G. O. Thomas, A. J. Sweetman and K. C. Jones, An input–output balance study for PCBs in humans, *Environ. Int.*, 2002, **28**(3), 203–214, DOI: [10.1016/S0160-4120\(02\)00030-2](https://doi.org/10.1016/S0160-4120(02)00030-2).
- 53 M. Schwenk, T. Gabrio, O. Pöpke and T. Wallenhorst, Human biomonitoring of polychlorinated biphenyls and polychlorinated dibenzodioxins and dibenzofurans in teachers working in a PCB-contaminated school, *Chemosphere*, 2002, **47**(2), 229–233, DOI: [10.1016/S0045-6535\(01\)00307-1](https://doi.org/10.1016/S0045-6535(01)00307-1).
- 54 H. Kodama and H. Ota, Transfer of polychlorinated biphenyls to infants from their mothers, *Arch. Environ. Health Int. J.*, 1980, **35**(2), 95–100, DOI: [10.1080/00039896.1980.10667472](https://doi.org/10.1080/00039896.1980.10667472).
- 55 D. Megson, G. O'Sullivan, S. Comber, P. J. Worsfold, M. C. Lohan, M. R. Edwards, W. J. Shields, C. D. Sandau and D. G. Patterson Jr, Elucidating the structural properties that influence the persistence of PCBs in humans using the National Health and Nutrition Examination Survey (NHANES) dataset, *Sci. Total Environ.*, 2013, **461–462**, 99–107, DOI: [10.1016/j.scitotenv.2013.04.082](https://doi.org/10.1016/j.scitotenv.2013.04.082).
- 56 C. L. Quinn and F. Wania, Understanding differences in the body burden–age relationships of bioaccumulating contaminants based on population cross-sections versus individuals, *Environ. Health Perspect.*, 2012, **120**, 554–559, DOI: [10.1289/ehp.1104236](https://doi.org/10.1289/ehp.1104236).
- 57 A. Geisler, L. Oemisch, S. Endo and K.-U. Goss, Predicting storage–lipid water partitioning of organic solutes from molecular structure, *Environ. Sci. Technol.*, 2015, **49**(9), 5538–5545, DOI: [10.1021/es506336m](https://doi.org/10.1021/es506336m).
- 58 U. Schenker, M. MacLeod, M. Scheringer and K. Hungerbühler, Improving data quality for environmental fate models: a least-squares adjustment procedure for harmonizing physicochemical properties of organic compounds, *Environ. Sci. Technol.*, 2005, **39**(21), 8434–8441, DOI: [10.1021/es0502526](https://doi.org/10.1021/es0502526).
- 59 K. Martinez-Guryn, N. Hubert, K. Frazier, S. Urlass, M. W. Musch, P. Ojeda, J. F. Pierre, J. Miyoshi, T. J. Sontag, C. M. Cham, C. A. Reardon, V. Leone and E. B. Chang, Small intestine microbiota regulate host digestive and absorptive adaptive responses to dietary lipids, *Cell Host Microbe*, 2018, **23**(4), 458–469.e5, DOI: [10.1016/j.chom.2018.03.011](https://doi.org/10.1016/j.chom.2018.03.011).
- 60 I. Semova, J. D. Carten, J. Stombaugh, L. C. Mackey, R. Knight, S. A. Farber and J. F. Rawls, Microbiota regulate



- intestinal absorption and metabolism of fatty acids in the zebrafish, *Cell Host Microbe*, 2012, **12**(3), 277–288, DOI: [10.1016/j.chom.2012.08.003](https://doi.org/10.1016/j.chom.2012.08.003).
- 61 H. Sato, L. S. Zhang, K. Martinez, E. B. Chang, Q. Yang, F. Wang, P. N. Howles, R. Hokari, S. Miura and P. Tso, Antibiotics suppress activation of intestinal mucosal mast cells and reduce dietary lipid absorption in Sprague-Dawley rats, *Gastroenterology*, 2016, **151**(5), 923–932, DOI: [10.1053/j.gastro.2016.07.009](https://doi.org/10.1053/j.gastro.2016.07.009).
 - 62 S. Devkota, Y. Wang, M. W. Musch, V. Leone, H. Fehlner-Peach, A. Nadimpalli, D. A. Antonopoulos, B. Jabri and E. B. Chang, Dietary-fat-induced taurocholic acid promotes pathobiont expansion and colitis in *Il10^{-/-}* mice, *Nature*, 2012, **487**(7405), 104–108, DOI: [10.1038/nature11225](https://doi.org/10.1038/nature11225).
 - 63 E. Y. Huang, V. A. Leone, S. Devkota, Y. Wang, M. J. Brady and E. B. Chang, Composition of dietary fat source shapes gut microbiota architecture and alters host inflammatory mediators in mouse adipose tissue, *J. Parenter. Enteral Nutr.*, 2013, **37**(6), 746–754, DOI: [10.1177/0148607113486931](https://doi.org/10.1177/0148607113486931).
 - 64 L. A. David, C. F. Maurice, R. N. Carmody, D. B. Gootenberg, J. E. Button, B. E. Wolfe, A. V. Ling, A. S. Devlin, Y. Varma, M. A. Fischbach, S. B. Biddinger, R. J. Dutton and P. J. Turnbaugh, Diet rapidly and reproducibly alters the human gut microbiome, *Nature*, 2014, **505**(7484), 559–563, DOI: [10.1038/nature12820](https://doi.org/10.1038/nature12820).
 - 65 G. A. Moser and M. S. McLachlan, Modeling digestive tract absorption and desorption of lipophilic organic contaminants in humans, *Environ. Sci. Technol.*, 2002, **36**(15), 3318–3325, DOI: [10.1021/es015853l](https://doi.org/10.1021/es015853l).
 - 66 P. R. Holt and J. A. Balint, Effects of aging on intestinal lipid absorption, *Am. J. Physiol.*, 1993, **264**, G1–G6, DOI: [10.1152/ajpgi.1993.264.1.G1](https://doi.org/10.1152/ajpgi.1993.264.1.G1).
 - 67 A. Szymaszkiewicz, K. Szymaszkiewicz, J. Fichna and M. Zielińska, The age-related alterations in the enteric nervous system and their impact on peristalsis of the gastrointestinal tract, *Postepy Biochem.*, 2021, **61**(1), 34–43, DOI: [10.18388/pb.2021_367](https://doi.org/10.18388/pb.2021_367).
 - 68 L. Drozdowski, T. Woudstra, G. Wild, M. T. Clandinin and A. B. R. Thomson, Dietary lipids modify the age-associated changes in intestinal uptake of fructose in rats, *Am. J. Physiol. Gastrointest. Liver Physiol.*, 2005, **288**(1), G125–G134, DOI: [10.1152/ajpgi.00311.2003](https://doi.org/10.1152/ajpgi.00311.2003).
 - 69 T. Takasuga, K. Senthilkumar, H. Takemori, E. Ohi, H. Tsuji and J. Nagayama, Impact of FEBRA (fermented brown rice with *Aspergillus Oryzae*) intake and concentrations of PCDDs, PCDFs and PCBs in blood of humans from Japan, *Chemosphere*, 2004, **57**(10), 1409–1426, DOI: [10.1016/j.chemosphere.2004.08.082](https://doi.org/10.1016/j.chemosphere.2004.08.082).
 - 70 J. Parker, A. Branum, D. Axelrad and J. Cohen, Adjusting National Health and Nutrition Examination Survey sample weights for women of childbearing age, *Vital Health Stat.*, 2013, **2**(157), 1–20, https://stacks.cdc.gov/view/cdc/22068/cdc_22068_DS1.pdf.
 - 71 A. Sjödin, R. S. Jones, S. P. Caudill, L. Y. Wong, W. E. Turner and A. M. Calafat, Polybrominated diphenyl ethers, polychlorinated biphenyls, and persistent pesticides in serum from the National Health and Nutrition Examination Survey: 2003–2008, *Environ. Sci. Technol.*, 2014, **48**(1), 753–760, DOI: [10.1021/es4037836](https://doi.org/10.1021/es4037836).
 - 72 E. Fattore, R. Fanelli, E. Dellatte, A. Turrini and A. D. Domenico, Assessment of the dietary exposure to non-dioxin-like PCBs of the Italian general population, *Chemosphere*, 2008, **73**(1), S278–S283, DOI: [10.1016/j.chemosphere.2007.12.040](https://doi.org/10.1016/j.chemosphere.2007.12.040).
 - 73 P. H. Chen, M. L. Luo, C. K. Wong and C. J. Chen, Comparative rates of elimination of some individual polychlorinated biphenyls from the blood of PCB-poisoned patients in Taiwan, *Food Chem. Toxicol.*, 1982, **20**(4), 417–425, DOI: [10.1016/S0278-6915\(82\)80107-5](https://doi.org/10.1016/S0278-6915(82)80107-5).
 - 74 J. J. Ryan, D. Levesque, L. G. Panopio, W. F. Sun, Y. Masuda and H. Kuroki, Elimination of polychlorinated dibenzofurans (PCDFs) and polychlorinated biphenyls (PCBs) from human blood in the Yusho and Yu-Cheng rice oil poisonings, *Arch. Environ. Contam. Toxicol.*, 1993, **24**, 504–512, DOI: [10.1007/BF01146170](https://doi.org/10.1007/BF01146170).
 - 75 J. E. Snawder and J. C. Lipscomb, Interindividual variance of cytochrome P450 forms in human hepatic microsomes: correlation of individual forms with xenobiotic metabolism and implications in risk assessment, *Regul. Toxicol. Pharmacol.*, 2000, **32**, 200–209, DOI: [10.1006/rtp.2000.1424](https://doi.org/10.1006/rtp.2000.1424).
 - 76 L. Lind, J. Penell, A.-C. Syvänen, T. Axelsson, E. Ingelsson, A. P. Morris, C. Lindgren, S. Salihovic, B. van Bavel and P. M. Lind, Genetic variation in the CYP1A1 gene is related to circulating PCB118 levels in a population-based sample, *Environ. Res.*, 2014, **133**, 135–140, DOI: [10.1016/j.envres.2014.05.017](https://doi.org/10.1016/j.envres.2014.05.017).
 - 77 S. A. Wood, J. M. Armitage, M. J. Binnington and F. Wania, Deterministic modeling of the exposure of individual participants in the National Health and Nutrition Examination Survey (NHANES) to polychlorinated biphenyls, *Environ. Sci.: Processes Impacts*, 2016, **18**, 1157–1168, DOI: [10.1039/c6em00424e](https://doi.org/10.1039/c6em00424e).

