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Ecotoxicology of mercury in burbot (*Lota lota*) from interior Alaska and insights towards human health

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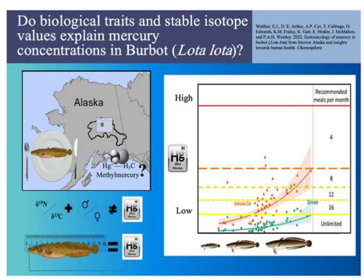
HIGHLIGHTS

- Burbot are an important sport and subsistence fish resource in parts of Alaska.
- Fish length was an effective predictor of [THg] in burbot muscle and liver.
- Stable isotope values and sex were not accurate predictors of [THg] in burbot.
- All burbot measured had [THg] within Alaskan consumption recommendations.

GRAPHICAL ABSTRACT



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ABSTRACT

Fish consumption has many health benefits, but exposure to contaminants, such as mercury (Hg), in fish tissue can be detrimental to human health. The Tanana River drainage, Alaska, USA supports the largest recreational harvest of burbot (*Lota lota*) in the state, yet information to evaluate the potential risks of consumption by humans is lacking. To narrow this knowledge gap, we sought to (i) quantify the concentrations of total Hg ([THg]) in burbot muscle and liver tissue and the ratio between the two tissues, (ii) assess the effect of age, length, and sex on [THg] in muscle and liver tissue, (iii) evaluate if [THg] in muscle tissue varied based on trophic information, and (iv) compare observed [THg] to consumption guidelines and statewide baseline data. The mean [THg] was 268.2 ng/g ww for muscle tissue and 62.3 ng/g ww for liver tissue. Both muscle [THg] and liver [THg] values were positively associated with fish length. Trophic information ($\delta^{15}N$ and $\delta^{13}C$) was not significantly related to measured [THg] in burbot muscle, which is inconsistent with typical patterns of biomagnification observed in other fishes. All burbot sampled were within the established categories for consumption recommendations determined by the State of Alaska for women of childbearing age and children. Our

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results provide the necessary first step towards informed risk assessment of burbot consumption in the Tanana drainage and offer parallels to fisheries and consumers throughout the subarctic and Arctic region.

1. Introduction

Human fish consumption is critical for providing global food security and sustaining nutrient-rich, healthy diets (Daviglus et al., 2002; Thilsted et al., 2014, 2016). The consumption of fish is beneficial for the neurodevelopment of infants and young children (Mozaffarian and Rimm, 2006), and is linked to reduced incidence of cardiovascular disease (Kris-Etherton et al., 2002) and the risk of stroke (Chowdhury et al., 2012). Some cultures and communities heavily rely on the consumption of locally-caught fish for a significant portion of their protein and energetic requirements (Hortle, 2007). For example, rural and largely Indigenous residents in Alaska consume an average estimated 71.5 kg of fish per person annually (Fall, 2016). Despite the known health benefits (Daviglus et al., 2002; Loring et al., 2010), fish consumption may also pose a risk because fish can contain harmful organic or inorganic environmental contaminants (Fraley et al., 2020; Gribble et al., 2016; Rodríguez-Hernández et al., 2016; Wang et al., 2013).

Mercury (Hg) is a notable contaminant found in fish that can negatively impact human health. Hg is a naturally occurring heavy metal found in cinnabar ore (HgS), and in trace amounts throughout the aquatic environment (Beckers and Rinklebe, 2017; Goldwater, 1971; Gworek et al., 2016; Ullrich et al., 2001). However, since the industrial revolution there has been a three-fold increase in atmospherically deposited Hg (Lindberg et al., 2007). Atmospheric transportation of Hg is considered one of the main factors that contributes to its ubiquitous occurrence in fishes (Jewett and Duffy, 2007). The methylation of inorganic Hg^{2+} into the more toxic monomethylmercury$^+$ ($MeHg^+$) form occurs through biotic and abiotic processes that vary across space and time affecting its availability in the ecosystem (Celo et al., 2006; Korthals and Winfrey, 1987). The predominant pathway for the absorption of $MeHg^+$ in fishes occurs in the gastrointestinal tract from diet, which then biomagnifies through the food chain. (Hall et al., 1997; Jewett and Duffy, 2007). In general, $MeHg^+$ accounts for greater than 85% of the total Hg (THg) present in fish muscle tissue (Cyr et al., 2019b; Jewett et al., 2003; Jewett and Duffy, 2007; Luten et al., 1980). In humans, $MeHg^+$ is more readily absorbed in the gastrointestinal tract compared to other forms of Hg and is readily transported to the brain (Jewett and Duffy, 2007).

Monomethylmercury$^+$ is a known environmental contaminant that has been associated with neurobehavioral and neurological deficiencies, as well as disrupting the development of cardiovascular homeostasis (Clarkson, 1990; Díez, 2008; Sørensen et al., 1999). The adverse effects of $MeHg^+$ are of particular concern to the developing fetus and to young children ; (Antunes dos Santos et al., 2016; Díez, 2008; Gilbert and Grant-Webster, 1995). $MeHg^+$ binds to cysteine and can biochemically mimic the essential amino acid methionine, which then enables the molecule to cross the placental and blood-brain barriers (Kerper et al., 1992). This direct access to neurological development enables $MeHg^+$ to disrupt antioxidant functions and the neuroendocrine system. Due to the disproportionate impact of $MeHg^+$ on the developing nervous system of infants and children, most fish consumption advisories focus on pregnant or nursing women, and young children (EPA, 2000; Gribble et al., 2016; Hamade, 2014).

Mercury concentrations ([Hg]) in fishes can vary among geographical regions, ecosystems, and species. Geographic location has been shown to be an important driver of [Hg] in freshwater (Cyr et al., 2017; Depew et al., 2013) and marine fishes (Cyr et al., 2019a), due to differences in biogeochemical processes across space that controls the local abundance of Hg available for methylation and subsequent absorption (Wiener et al., 2003). In addition, trophic position (Bentzen et al., 2016) and foraging niche (Le Croizier et al., 2019) can influence methylmercury concentrations ([$MeHg^+$]) found in fish tissues. For an individual fish, the accumulation of $MeHg^+$ is determined by its size, diet, and trophic position, bioaccumulating through time and biomagnifying through the food chain (Cyr et al., 2019b; Wiener et al., 2003). The change of stable isotope ratios of nitrogen ($\delta^{15}N$) and carbon ($\delta^{13}C$) has frequently been used to relate trophic position ($\delta^{15}N$) and foraging niche ($\delta^{13}C$) to total [Hg] ([THg]) in fish tissue (Liu et al., 2018). Differences in [THg] between sexes has also been observed for some species (Madenjian et al., 2015; McClain et al., 2006; Wiener et al., 2003), but is not consistent across species (Bastos et al., 2016; Gewurtz et al., 2011). Generally, fish species with greater [$MeHg^+$] are those with longer lifespans and highly piscivorous diets, such as northern pike (*Esox lucius)*, lake trout (*Salvelinus namaycush*) and burbot (*Lota lota)* in freshwater ecosystems (Depew et al., 2013; Jewett and Duffy, 2007). The spatial and biological variation of $MeHg^+$ highlights the importance of obtaining regionally- and species-specific data when assessing the health risks of fish consumption.

Burbot (*Lota lota*) are harvested for consumption across its Holarctic range (Stapanian et al., 2010). Relatively long-lived (McPhail and Paragamian, 2000) and a highly piscivorous diet (Chen, 1969) make burbot particularly susceptible to the bioaccumulation and biomagnification of $MeHg^+$(Lehnherr, 2014). While there has been some previous research in lentic systems (Madenjian et al., 2015; Power et al., 2002), to date little is known about how biological factors relate to [$MeHg^+$] in fluvial burbot. In Alaska, burbot are a desired species for both recreational and subsistence fisheries, with annual average harvest estimates of 3959 fish (Romberg et al., 2021). Burbot livers are a coveted delicacy among Arctic residents because they are rich in vitamins and fatty acids (Branion, 1930; Wong, 2011). The largest recreational fishery occurs in various portions of the Tanana River drainage near urban population centers, where burbot are targeted throughout the year (Wuttig and Baker, 2017). Due to the long history of mining activity, regional deposits of cinnabar, atmospheric deposition, and the semi-urban center of Fairbanks located along the Tanana River, there are public health concerns surrounding the use of burbot as a supplemental source of protein for many interior Alaskans (Metz, 1991; Fitzgerald et al., 2005). Whole body composite samples of burbot have been previously analyzed for [THg] from a limited sample size (n = 12) in Tanana River drainage (Hinck et al., 2006, Table 1). However, information is lacking on tissue-specific [$MeHg^+$] in burbot from the Tanana River drainage. The THg assay following EPA method 7473 is a fast and efficient method for quantifying all Hg species present in fish muscle tissue. Over 85% of THg present in muscle tissue of most fish species is in the $MeHg^+$ form, making the THg assay an excellent technique for quantifying $MeHg^+$ in fish tissue (Bloom, 1992; Cyr et al., 2019b; Jewett et al., 2003). In this paper, we measured THg and bulk stable isotopes of carbon and nitrogen in burbot from the Tanana River drainage, Alaska. Our objectives were to (i) quantify the [THg] in burbot muscle and liver tissue, and the ratio of [THg] between the two tissues, (ii) assess the effect of age, sex, and length on [THg] in muscle and liver tissue, (iii) evaluate if [THg] in muscle tissue varied based on bulk $\delta^{15}N$ and $\delta^{13}C$ values, and (iv) compare [THg] to consumption guidelines and current statewide baseline data. Understanding these relationships can describe how the ecology and biology of burbot influence the concentration of THg and provide information for consumers evaluating potential health risks associated with burbot harvested from the Tanana River drainage.

2. Materials and methods

2.1. Study area

The Tanana River is a turbid, sub-arctic, glacially fed river draining 73,898 km^2 that originates in the Alaska Range and the Wrangell Mountains, flows 940 km, and eventually joins the Yukon River. The city of Fairbanks is located on the Chena River, a clear-water tributary of the Tanana River. Fairbanks is the most populous community in interior Alaska and the Tanana River drainage. Nearby communities in the Tanana River drainage include multiple military installations, rural towns, and Indigenous villages. Many residents from Fairbanks and these surrounding communities participate in a popular burbot fishery. Additionally, burbot are harvested from Healy Lake as part of a predominately subsistence fishery (Brown et al., 2016). For this study, burbot were collected from urban to semi-urban portions of the Tanana River drainage (Fig. 1), which contains over 85% of the nearly 100,000 residents within the drainage (Baker, 2018).

2.2. Sample collection

Burbot were collected from December 2018 to November 2019 near public access and established fishing areas (Fig. 1). Burbot were captured primarily using baited setlines deployed in water depths of 0.3–5.0 m during the open water season (April to October), and through the ice during winter months (November to March). For details on capture methods, see Supplementary Material Fig. S1. Smaller burbot (<200 mm) were collected opportunistically from another study in the drainage using baited minnow traps (Gee's G40 wire minnow trap) with 5.7 cm opening and 0.6 cm mesh. Upon capture, burbot were handled with nitrile gloves and immediately euthanized by applying blunt force trauma to the head, in accordance with the approved University of Alaska Institutional Animal Care and Use Committee (IACUC) permit 1346016-3. Burbot were individually wrapped in Control Company Ultra-Clean™ Supreme Aluminum Foil (VWR International) and stored in a 4.08L Whirl-pak™ bag. The sampling location and capture date was recorded for each sampled burbot. Whole burbot were stored in a −30 °C freezer until sample preparation occurred.

2.3. Sample preparation and biological data collection

Frozen burbot were thawed and removed from the aluminum foil. Total length (mm) and body mass (g) were recorded for each burbot. A sterile scalpel was used to cut into the musculature on the left side of each burbot and remove two 5 g muscle samples (skin removed) from above the lateral line between the first dorsal fin and the head. One muscle tissue sample was used for THg analysis and the other for stable isotope analysis. Approximately 5 g of liver was subsampled for THg analysis. Sex was determined for each fish by visually inspecting the gonads. Both sagittal otoliths were removed, cleaned, dried, and stored in a coin envelope for aging.

Age estimation was performed using the crack-and-burn method (Chilton and Beamish, 1982; Evanson, 2000). Each otolith was either broken or cut in half through the nucleus. Aging was primarily conducted using the right otolith from each burbot, while the left otolith was used to verify readings. Otoliths were heated on a hot plate until the cracked edge was charred. The cracked edge of the otolith was sanded and then polished with 2000 grit sandpaper. Otoliths were viewed under

Table 1
Summary of the mean length, age, sex (M: male, F: female, U: unknown), and the geometric mean [THg] in burbot muscle ($n = 50$) and liver tissue ($n = 46$) collected across the Tanana River drainage, Alaska, USA, between 2018 and 2019. [THg] values from this study are compared to previously documented [THg] values of burbot from the Arctic.

Study area (source)	Sample location	Sample size	Length (SD)	Median age	Sex	Mean muscle [THg] (SD)	Mean liver [THg] (SD)
Tanana River drainage, AK (this study)	Chena River	18	494 (±129)	6	M: 4 F: 8 U: 6	387.0 (±1.5)	91.8 (±1.7)
	Tanana River	18	527 (±135)	6	M: 11 F: 6 U: 1	253.1 (±2.0)	55.9 (±2.8)
	Pile Driver Slough	3	467 (±100)	5	M: 3 F: 0 U: 0	190.4 (±2.0)	31.1 (±1.8)
	Nenana River	2	502 (±209)	6	M: 0 F: 2 U: 0	217.4 (±2.9)	49.8 (±3.9)
	Healy Lake	4	674 (±78)	10	M: 1 F: 3 U: 0	341 (±1.5)	–
	Middle Fork Chena River	4	167 (±47)	3	M: 1 F: 2 U: 1	84.2 (±1.4)	28.4 (±1.2)
	McManus Creek	1	294	4	M: 0 F: 1 U: 0	174.4	54.1
Total:		50	489 (±163)	6	M: 20 F: 22 U: 8	268.2 (±2.0)	62.3 (±2.3)
Russian Arctic rivers (Pelletier et al., 2017)	–	2135	872	–	–	104–171[a]	–
Yukon-Kuskokwim delta, AK (Duffy et al., 1999)	–	3*	–	–	–	96 (±5)[b]	–
Yukon River, AK (Hinck et al., 2006)	Fairbanks	12	M: 589 (±65) F: 700 (±62)	M: 9.5 (±2.1)[b] F: 10.6 (±1.1)[b]	M: 4 F: 8 U: 0	260[c]	–
	Kotlik	1	565	7	M: 1 F: 0 U: 0	130[c]	–
Upper Tanana River (Matz et al., 2005)		10	>400 mm[d]	–	–	734 (±340)[b]	
Middle Kuskokwim River, AK (Matz et al., 2017)	–	118	615 (±82)	–	–	140 (±120)[b]	–
	–	54	534 (±79)	6	–	160 (±120)[b]	40 (±40)[b]

[a] Range of geometric mean [THg] measured in burbot muscle tissue across the study period between 1988 and 2001.
[b] Arithmetic mean (standard deviation).
[c] Least-squares mean from composite samples.
[d] Length measurements for all individuals from this study were not available, but the study lead author confirmed all sampled burbot were above 400 mm (A. Matz, personal communication).

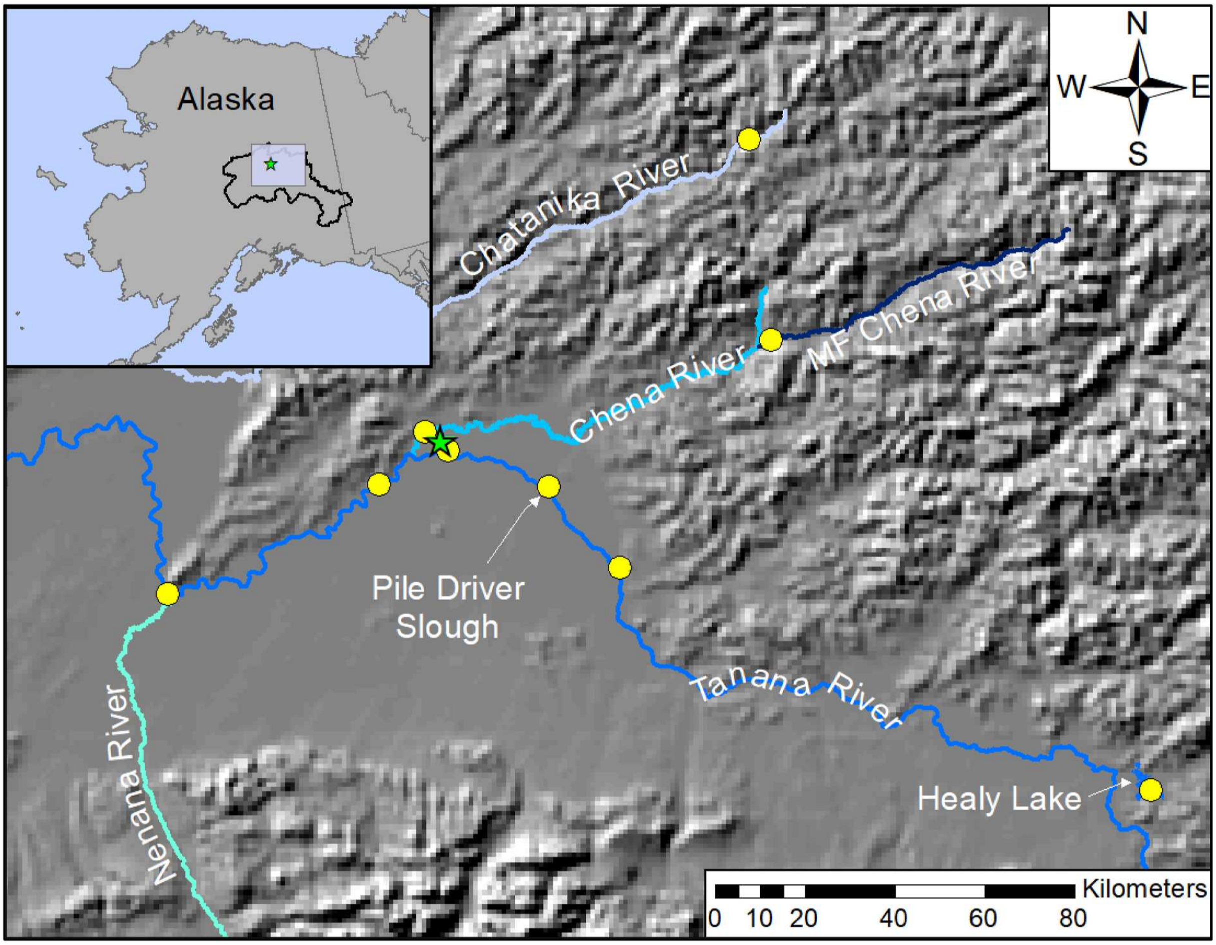

Fig. 1. Map of the region of the Tanana River drainage, Alaska, USA sampled for burbot. The watershed boundary of the Tanana River drainage is bolded in black and the location of the focal map is identified by the purple polygon in the inset map of Alaska. The green star is the location of Fairbanks, Alaska (64.83, −147.84). Yellow dots represent sample locations from the seven water bodies monitored (*n = number of burbot collected from each water body*): Chena River ($n = 18$); Tanana River (3 sampling locations, $n = 18$); Pile Driver Slough ($n = 3$); Nenana River ($n = 2$); Healy Lake ($n = 4$); Middle Fork Chena River ($n = 4$); McManus Creek (tributary to the Chatanika River, $n = 1$). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

a Leica M165C stereoscope (Leica Microsystems, Wetzlar, Germany) with reflected light at 20-40X power and photographs were captured with a mounted Leica DFC 450 camera using an automated image capture software Leica Application Suite (LAS). Ages were estimated independently by two trained readers. The two readers worked to resolve any discrepancy and come to an agreement on fish age. If a consensus on an age was reached, it was reported as a final resolved age, and if a consensus was not reached, ages were omitted.

2.4. THg analysis

Each muscle and liver sample was weighed (g) and freeze dried (Labcono, FreeZone 4.5 L) for a minimum of 48 h. Samples were reweighed after drying to calculate percent water in each tissue. Tissue samples were homogenized into a fine powder using a CryoMill ball grinder for 2 min. Approximately 0.010–0.025 g of sample was analyzed using a Milestone DMA-80 instrument (U.S. EPA method #7473-EPA30B). [THg] were reported as parts per billion (ng/g) wet weight (ww) based on the percent water previously calculated. Quality assurance and quality control measures were assessed based on blanks, a 100 ng/g $HgCl_2$ liquid standard, and two standard reference materials, DORM-4 (National Resource Council Canada; 0.354 ± 0.031 mg/kg) and DOLT-5 (Dogfish liver, National Resource Council Canada; 0.44 ± 0.18 mg/kg) (Cyr et al., 2017). Mean percent recoveries for each standard reference material were: 100 ng/g, 109.5 ± 3.1%; DORM-4, 93.1 ± 3.7%; and DOLT-5, 105.5 ± 7.7%. All samples were analyzed in duplicate and the resulting THg concentrations were averaged. Coefficient of variation (CV) between replicates was ≤ 15%.

2.5. Stable isotope analysis

To make inferences regarding Hg concentrations in tissues and burbot trophic status within the Tanana River drainage, nitrogen and carbon stable isotope analyses were conducted on each fish sampled to calculate indices for relative trophic position ($\delta^{15}N$) and foraging niche ($\delta^{13}C$) (Fraley et al., 2021). Because fish sampled were of the same species, captured within the same river drainage, and collected during a short window of time, bulk $\delta^{15}N$ information is a defensible index for trophic position for within-study comparisons, without the need for a baseline consumer correction (Fraley et al., 2021). Therefore, throughout the remainder of this paper, the terms $\delta^{15}N$ and “relative trophic position” are used interchangeably.

To achieve this, muscle samples were dried in a drying oven for at least 36 h between 55 and 60 °C. Samples were ground to a homogenous powder with mortar and pestle, weighed to 0.3–0.6 mg, and analyzed using a ConFlow IV EA-IRMS (Elemental Analyzer Isotope Ratio Mass Spectroscopy) at the Alaska Stable Isotope Facility. Stable isotope ratios are expressed as per mil (‰) relative to Vienna Pee Dee Belemnite (VPDB) for $\delta^{13}C$ values and atmospheric nitrogen (Air) for $\delta^{15}N$ values. Stable isotope ratio was estimated as follows:

$$\delta^{13}C \ or \ \delta^{15}N \quad = \left(\frac{R_{Sample}}{R_{Standard}} - 1\right) * 1000 \quad (1)$$

where R_{Sample} is the ratio of the heavy to light isotope ($^{13}C/^{12}C$, or $^{15}N/^{14}N$) measured for that element in the burbot tissue sample, and $R_{Standard}$ is the ratio of the heavy to light isotopes in the standard used, VPDB or Air (Peterson and Fry, 1987).

Lipids are enriched in ^{12}C relative to proteins, therefore lipids can lower $\delta^{13}C$ values (DeNiro and Epstein, 1978; Post et al., 2007). Lipids were not extracted from tissues prior to stable isotope analysis. However, we examined C:N ratios, which are an effective proxy for lipid content, and determined that C:N ratios of these burbot were near the acceptable ratio for protein and carbohydrates of 3.7 (mean = 3.91, SD = 0.62, n = 46). As a result, $\delta^{13}C$ values for burbot muscle tissue were not lipid-corrected.

2.6. Statistical analysis

All analyses were performed using the statistical software R, version 3.6.1 (R Core Team, 2019). Prior to analysis, Pearson's correlation coefficient was calculated to test for correlation between age and total length among samples where data on both biological attributes were available ($n = 37$). There was a strong correlation between age and total length ($\rho = 0.90$), thus total length was used as a proxy for age to maximize sample size and age was not included in the subsequent analysis. A natural log transformation of [THg] was used to improve the normality of data and meet assumptions of homoscedasticity in residuals for regression analysis. The effect of sex on [THg] in burbot muscle and liver tissues was analyzed separately from other biological and environmental covariates because sex was not successfully determined for 8 out of the 50 burbot. An analysis of covariance (ANCOVA) using Type II sum of squares was performed to compare the difference in log-transformed [THg] in burbot muscle and liver between sexes, after controlling for fish total length. Various regression models were explored to assess the effect of biological characteristics on [THg], including length, sample location, and capture date. First, general additive models (GAMs) were developed to visually explore potential non-linearity in the response variable, log([THg]). Additionally, linear models of reduced complexity were developed to compare to GAMs. Using the small sample version of Akaike Information Criterion (AICc), a simple linear regression between [THg] and total length was selected as the most parsimonious model that best explained the data based on the lowest AICc value (Table S1). The slopes of the [THg]-length relationship were used as an indicator of the THg bioaccumulation factor in burbot tissue, such that a non-zero positive slope would be interpreted as being consistent with bioaccumulation. We examined the relationship between [THg] and $\delta^{15}N$ using an ANCOVA to control for total length and sample season. The sample season assigned to each burbot was based on the capture date and defined as: Spring (March–May), Summer (June–August), Fall (September–November), and Winter (December–February). All p-value statistical tests were compared at an $\alpha = 0.05$. The liver [THg] to muscle [THg] ratio was calculated for each individual burbot as the quotient of the liver [THg] divided by muscle [THg].

2.7. Comparison of [THg] to consumption guidelines

Mean muscle and liver [THg] for burbot from the Tanana River drainage were compared to the State of Alaska Department of Health and Human Services (SOA DHSS) fish consumption guidelines. These guidelines were established to provide consumption recommendations for women of childbearing age and children; there are no recommendations or restrictions for any other fish consumer groups. These guidelines use a risk-based approach to calculate monthly meal recommendations based on an assumed 6-ounce meal size, and an acceptable daily dose of 0.56 μg of Hg/kg body weight/day. There are five defined categories, ranging from the unlimited consumption category (0–200 ng/g ww), to the recommendation of four meals per month (680–1360 ng/g ww). The SOA consumption guidelines are intended for muscle tissue, and guidelines have not been established for liver tissue in Alaska. Therefore, for comparisons in this study, we use the muscle guidelines established by SOA DHSS as a surrogate for liver comparisons. Results from the guideline comparisons were reported as a percentage of samples within each category the guideline levels by tissue type. Additionally, the results from this study were compared to previously reported means for burbot around Alaska, including from the SOA Department of Environmental Conservation (DEC) Fish Monitoring Program. Burbot liver [THg] was directly compared to previously documented results (Matz et al., 2017).

3. Results

3.1. Quantification of [THg] in burbot muscle and liver

A total of 50 burbot were captured across the Tanana River drainage. The total length and mass of burbot analyzed for [THg] varied considerably, ranging from 116 to 840 mm (mean = 489 mm, SD = 163 mm) and from 9.0 to 3188.0 g (mean = 866.4 g, SD = 735.5 g). The geometric mean [THg] for muscle tissue ($n = 50$) was over four times greater than the geometric mean [THg] for live tissue ($n = 46$). Fish length, age, and [THg] in muscle and liver tissue varied among sample locations, but unequal sample sizes precluded statistical comparisons among locations (Table 1). The mean liver [THg] to muscle [THg] ratio was 0.26 ± 0.11 and ranged from 0.10 to 0.57.

3.2. Relationship between [THg] and burbot sex and fish length

After controlling for length, there was no statistical difference in the mean [THg] between male and female burbot in muscle tissue ($n = 42$; $F = 0.094$, $p = 0.761$) or liver tissue ($n = 38$; $F = 1.179$, $p = 0.285$). Mean [THg] in muscle tissue was four times greater than mean [THg] in liver tissue for the mean length of burbot (489 mm). Fish length explained 40.2% of the variation in [THg] in the muscle tissue ($p < 0.001$) and mean [THg] increased by 2.7% for each one cm increase in fish length. Fish length explained 30.1% of the variation in [THg] in the liver tissue ($p < 0.001$) and mean [THg] increased by 3.1% for each one cm increase in fish length (Fig. 2).

3.3. Burbot $\delta^{15}N$ and $\delta^{13}C$ values related to [THg]

Bulk $\delta^{15}N$ and $\delta^{13}C$ values were measured in muscle tissue of 44 burbot. Bulk $\delta^{15}N$ values averaged 9.28 ± 1.58‰ in burbot muscle tissue and ranged from 5.96‰ to 12.65‰. Bulk $\delta^{13}C$ values averaged −30.8 ± 2.82‰ in burbot muscle tissue and ranged from −38.0‰ to −26.4‰ (Fig. 3). After controlling for length and season we observed a weak correlation between [THg] in muscle tissue and $\delta^{15}N$ values ($F = 3.23$, $p = 0.08$) and no correlation between [THg] in muscle tissue and $\delta^{13}C$ values ($F = 0.23$, $p = 0.63$). In addition, after controlling for length of fish there was no significant effect of season on $\delta^{15}N$ ($F = 1.07$, $p = 0.35$) and $\delta^{13}C$ values ($F = 1.26$, $p = 0.27$).

3.4. Comparison of measured [THg] to fish consumption guidelines

To place into context and link to human relevance, all of the burbot measured in this study had [THg] that were within each of the SOA DHSS fish consumption categories developed for women of childbearing age and children (Table 2). The mean [THg] of these burbot is within the 16 meals per month consumption category. Individually, 32% of muscle samples and 89% of liver samples were within the unlimited consumption category, while 4% of muscle samples and 0% of liver samples were within the 4 meals per month category (680–1360 ng/g ww; Hamade, 2014). The mean muscle [THg] in burbot from the Tanana River drainage of 325.5 ng/g ww was similar to the statewide mean muscle

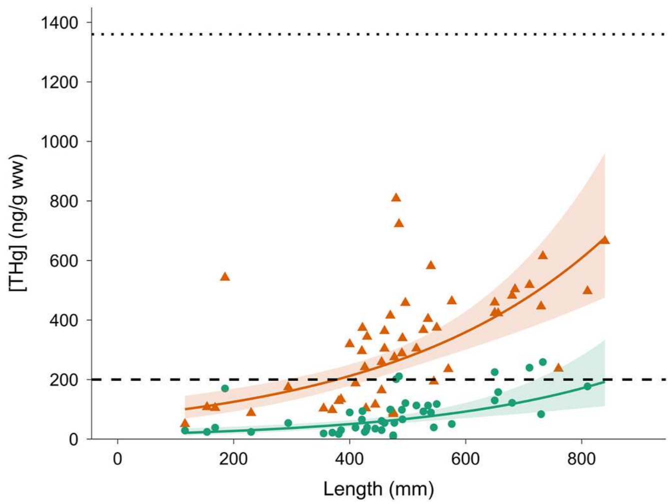

Fig. 2. Linear regression of total mercury concentration ([THg]) and length in burbot muscle tissue ($R^2 = 0.40$, $p < 0.001$) and burbot liver tissue ($R^2 = 0.30$, $p < 0.001$) collected between 2018 and 2019 in the Tanana River drainage, Alaska. Bolded green line represents the mean predicted [THg] in burbot liver tissue and the green ribbon represents the 95% confidence interval; green circles represent the observational [THg] in sampled burbot liver tissue ($n = 46$). Bolded orange line represents the mean predicted [THg] in burbot muscle tissue and the orange ribbon represents the 95% confidence interval; orange triangles represent the observational [THg] in sampled burbot muscle tissue ($n = 50$). Dashed black line represents the State ofAlaska Department of Health and Social Services (SOA DHSS) unlimited consumption advisory threshold of 200 ng/g ww for women of childbearing age and children. Dotted black line represents the upper limit of the SOA DHSS four meals per month consumption category (680–1360 ng/g ww). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

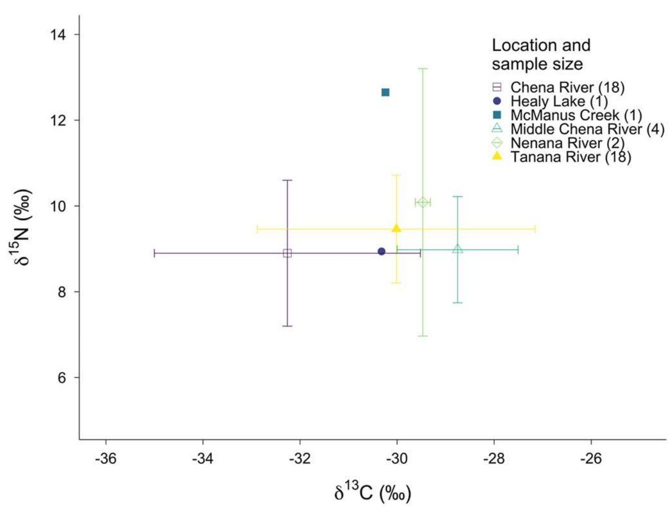

Fig. 3. Mean bulk $\delta^{13}C$ (‰) and $\delta^{15}N$ (‰) stable isotope values in burbot muscle from sample locations in the Tanana River drainage, AK. Error bars represent ±SD.

[THg] in burbot reported by the SOA DEC Fish Monitoring Program of 338 ng/g ww (Alaska Department of Environmental Conservation, 2020). The SOA DEC does not report liver [THg] for comparison. However, burbot liver [THg] measured in the Tanana River drainage are higher than liver [THg] reported in the Middle Kuskokwim River (40 ng/g ww, Matz et al., 2017, Table 1).

Table 2
Count (percent of total samples) of burbot muscle tissue ($n = 50$) and liver tissue ($n = 46$) within each consumption guideline category established by the State of Alaska Department of Health and Human Services (SOA DHSS). Burbot were collected from the Tanana River drainage, Alaska, USA, between December 2018 and November 2019. Consumption guidelines have not been established for liver tissue in Alaska. Therefore, we use the muscle tissue guidelines established by SOA DHSS as a surrogate for liver tissue.

Tissue Type	Consumption rate	Count (%)	[THg] range
Muscle	Unlimited	16 (32)	0–200 ng/g
	16 meals/month	11 (22)	200–340 ng/g
	12 meals/month	12 (24)	340–460 ng/g
	8 meals/month	9 (18)	460–680 ng/g
	4 meals/month	2 (4)	680–1360 ng/g
Liver	Unlimited	41 (89)	0–200 ng/g
	16 meals/month	5 (11)	200–340 ng/g
	12 meals/month	0 (0)	340–460 ng/g
	8 meals/month	0 (0)	460–680 ng/g
	4 meals/month	0 (0)	680–1360 ng/g

4. Discussion

In this paper, we examined [THg] in a widely caught and culturally important fish species from the Tanana River drainage, Alaska, and assessed potential biological variables and trophic dynamics that influenced measured [THg]. Our results revealed that fish length, which is a proxy for age, best explains the variance in [THg] in burbot muscle and liver tissue, while relative trophic position ($\delta^{15}N$ values) and foraging niche ($\delta^{13}C$ values) did not exhibit a significant relationship with measured [THg]. All the muscle and liver samples were within the SOA DHSS established consumption recommendations for $MeHg^+$. For specific guidance, sensitive groups of people (e.g., pregnant women and children) should refer to state consumption recommendations based on acceptable daily dosage of $MeHg^+$.

4.1. [THg] in burbot muscle and liver

On average, [THg] was four times greater in muscle than liver; this equates to liver [THg] to muscle [THg] ratios of less than one (mean: 0.26, SD: 0.11). This ratio has been used as a metric for biomonitoring of THg contamination in aquatic food webs, where high liver to muscle ratios have been associated with high levels of environmental contamination (Havelková et al., 2008). Lower [THg] in liver than muscle has been observed in many fish species, including sculpins (Family Cottidae, Harley et al., 2015), largemouth bass (*Micropterus salmoides*, Cizdziel et al., 2003), and various cod species (*Gadus* spp., Burger and Gochfeld, 2007; Kwaśniak and Falkowska (2012). It is proposed that the liver [THg] to muscle [THg] ratio will be low when muscle [THg] is below the hypothesized tissue saturation threshold, (>1000 ng/g; Cizdziel et al., 2003; Goldstein et al., 1996; Havelková et al., 2008), above which deposition of THg will shift to the liver. All muscle [THg] observed in Tanana River drainage burbot were below the hypothesized 1000 ng/g threshold at which $MeHg^+$ is hypothesized to be demethylated and then preferentially deposited in the liver as inorganic Hg or bound to selenium as the mercury selenide complex, HgSe (tiemenite: Goldstein et al., 1996). Liver [THg] to muscle [THg] ratios of burbot were low and all muscle [THg] were below 1000 ng/g, suggesting that the [Hg] in the environment and/or exposure in the Tanana River are insufficient to saturate burbot muscle tissue and cause high levels of THg accumulation in the liver.

4.2. Relationship between [THg] and biological characteristics

Of the biological characteristics examined as predictors of [THg] in burbot tissue, length, which is a proxy for age, was positively associated with [THg], but [THg] was not significantly different between sexes. Other research has revealed differences in [THg] between sexes in many fishes, including burbot (Madenjian et al., 2015). However, the effect of sex on [THg] is inconsistent across species (Bastos et al., 2016). Our results, as well as mixed findings in the literature (Bastos et al., 2016 Gewurtz et al., 2011), show that sex is an unreliable indicator for evaluating and understanding [THg] in fish. The general increase of [THg] in larger and older burbot is consistent with the THg accumulation observed in other fishes (Cizdziel et al., 2003; Cyr et al., 2019a). The variation of burbot [THg] explained by total length was comparable to other freshwater species in Alaska including the muscle of northern pike ($R^2 = 0.44$; Jewett et al., 2003) and whitefish ($R^2 = 0.41$; Jewett et al., 2003). These results indicate that larger (and older) individual burbot in the Tanana River drainage likely have higher [THg] in contrast to smaller (and younger) individuals.

4.3. $\delta^{15}N$ and $\delta^{13}C$ values related to [THg]

Burbot muscle [THg] was not associated with relative trophic position, as estimated by $\delta^{15}N$ values. Although burbot in the Tanana and Yukon River drainages become progressively more piscivorous with age (Chen, 1969), this species is opportunistic and will continue to feed on invertebrates and smaller prey throughout their life (e.g.- Petromyzontidae; Chen, 1969; McPhail and Paragamian, 2000). The opportunistic nature of burbot feeding could introduce variability in observed $\delta^{15}N$ values, which could confound the relationship between relative trophic position and [THg]. Further, limitations have been recognized with the use of bulk nitrogen isotopes for accurately estimating trophic level. For example, trophic enrichment factors can vary by species both physiologically and ecologically, and the lack of a baseline used to standardize trophic position precludes robust comparisons between fish caught at different locations (Hannides et al., 2009; McCutchan et al., 2003; O'Reilly et al., 2002; Vander Zanden and Rasmussen, 2001). However, because the fish collected for this study are all of one species, were collected within a single river drainage, and from a short window of time, bulk $\delta^{15}N$ is a suitable index for comparing trophic information within this investigation (Fraley et al., 2021). Compound specific stable isotope analysis for some amino acids, such as phenylalanine and glutamic acid, are useful for accurately estimating trophic level because phenylalanine is highly conserved as it passes through consumers and represents the isotopic signature of basal primary producers while glutamic acid enriches with each level of consumer (Chikaraishi et al., 2009). The use of compound specific amino acid stable isotope analysis could provide additional clarity in understanding the trophic status of Tanana River burbot and the possible influence of feeding ecology on the accumulation of Hg.

Our data indicate that burbot from the Tanana River drainage may be using foraging locations with different sources of carbon. For example, burbot from the Middle Chena River and main stem Chena River had muscle $\delta^{13}C$ values noticeably lower (mean = −34.3‰ and −31.8‰, respectively) than those expected for a piscivorous fish from a subarctic freshwater environment exhibiting given $\delta^{15}N$ values (Cott et al., 2011; Recknagel et al., 2015). These low $\delta^{13}C$ values could be indicative of methanogenesis-based primary production (Conrad and Claus, 2005; Whiticar, 1999), because methane-oxidizing bacteria have lower $\delta^{13}C$ values than photosynthetic algae at the base of the food web. Owing to the migratory behavior of Tanana River burbot (Evanson, 2000) and hotspots of methane-based productivity in the Tanana River drainage (Clilverd et al., 2008), access to these and other distinct food webs might have influenced our inability to detect strong relationships between [THg] and foraging niche or relative trophic position. Further investigation into the feeding ecology in this region is needed to better understand how burbot may utilize different food webs seasonally throughout the drainage. This could be achieved by further stable isotope analysis (i.e., establishing baselines to calculate trophic positions comparable across locations and time periods) and studies on burbot diet composition in the Tanana River drainage.

4.4. Fish consumption comparisons

Total mercury concentrations in Tanana River burbot tissues were compared with the SOA DHSS fish consumption guidelines. The intent of these guidelines is focused on balancing the benefits versus risks of fish consumption. Dose of $MeHg^+$ is the key linkage between risk of exposure and consumption. Therefore, to balance this, SOA DHSS unlimited consumption guideline is set at 200 ng/g for women of childbearing age and children. Below this guideline level, SOA DHSS recommends that consumption can be unlimited with regards to risk from $MeHg^+$. Above the guideline, the SOA DHSS recommends reduced consumption frequency (i.e. meals per month of 6-ounce servings) for women who are or may become pregnant, women who are breastfeeding, or young children.

Mean [THg] for all burbot muscle samples was within the consumption category recommending 16 meals per month for pregnant women and children. Individually, all burbot muscle samples were within the established SOA DHSS consumption categories, and the greatest number of samples ($n = 16$) were within the unlimited consumption category (Hamade, 2014). Nearly all burbot liver samples (89%) were below the SOA DHSS unlimited consumption guideline level and can be consumed with minimal concern for $MeHg^+$ exposure. This is important considering that burbot livers are a source of fatty acids and vitamins K and D (Branion, 1930; Wong, 2011) and are considered a delicacy across Arctic communities. However, given the importance of the liver in storage and transformation of contaminants, consumers should consider the risk from other contaminants when consuming burbot liver (e.g., organohalogens, Fraley et al., 2020; Mueller and Matz, 2000), and should always consult local and species-specific consumption advisory information. The remainder of the burbot liver samples are all within the consumption category recommending up to 16 meals per month. Because of the well-established benefits of consuming wild fish (Daviglus et al., 2002; Loring et al., 2010), women and children can supplement burbot with other fish species that are known to have low levels of [THg] (e.g., Pacific salmon, *Oncorhynchus* spp., mean = 47 ng/g; Sheefish (*Stenodus leucicthys*), mean = 138 ng/g; Arctic grayling (*Thymallus arcticus*), mean = 86 ng/g; Alaska Department of Environmental Conservation, 2020).

The mean muscle [THg] in burbot from the Tanana River drainage was comparable to the statewide mean muscle [THg] in burbot reported by the SOA DEC Fish Monitoring Program (2020). However, mean [THg] in burbot muscle tissue from this study was greater than the mean [THg] of 160 ng/g documented in burbot muscle from the lower Kuskokwim River (Matz et al., 2017) and 260 ng/g whole body composite samples from the Tanana River drainage (Hinck et al., 2006), indicative of variation of [THg] in burbot among watersheds in Alaska. Conversely, mean muscle [THg] in burbot from this study was lower than the mean muscle [THg] of 734 ng/g for 10 burbot collected from the upper Tanana River between 1987 and 1992 (Matz et al., 2005). It is worth noting that Duffy et al. (1999) and Hinck et al. (2006) analyzed THg in a small number of samples ($n = 3$ and $n = 12$, respectively), which makes comparisons tenuous. The mean muscle [THg] in burbot from this study was more than double the mean muscle [THg] of burbot sampled in 2001 from eight rivers across the Russian Arctic region (Pelletier et al., 2017), which may be a result of the naturally high [THg] in the Yukon River watershed (Zolkos et al., 2020). Local environmental factors that influence Hg availability and methylation are variable across watersheds, resulting in a wide degree of variation and range in [THg]. Despite [THg] of many fish being below the SOA DHSS guidelines for consumption, [THg] in burbot from the Tanana River drainage, and Alaska in general, are among the highest of all reported freshwater fishes in Alaska with the exception of lake trout (mean = 353 ng/g) and northern pike (mean = 396 ng/g, Alaska Department of Environmental

Conservation, 2020). Given the heterogeneity of [THg] in burbot across Alaska, low sample sizes in previous studies, and the relative high concentration with respect to other freshwater Alaskan fish, continued monitoring and research of THg in Tanana River burbot and from throughout the state is warranted. This is particularly important in areas with Hg point sources (e.g., mines; Gray et al., 2000), in addition to the expected increase in Holarctic Hg releases due to thawing permafrost (Schaefer et al., 2020) and more frequent wildfires (Giesler et al., 2017).

4.5. Summary

Total mercury concentrations in burbot from the Tanana River drainage were quantified to explore biological and ecological mechanisms for increased accumulations and to compare against the SOA DHSS fish consumption guidelines. [THg] in burbot varied by tissue type and increased with length. However, [THg] did not differ between sexes. Concentrations in muscle tissue were markedly higher than liver tissue, as evident by the low liver [THg] to muscle [THg] ratio across all samples. [THg] was not associated with $\delta^{15}N$, but $\delta^{13}C$ values provided evidence that burbot may be utilizing various unique food webs throughout the Tanana River drainage, which could confound the relationship between relative trophic position and [THg]. A model including total length alone best explained the variation in [THg] in both tissues based on AICc model selection criterion and parsimony. Finally, we note that all of the burbot from this study had [THg] within the SOA DHSS established consumption categories for young children, and pregnant or nursing women. Fish consumers who are concerned about their fish or have additional questions should consult their local public health entities for species and site-specific concerns.

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Data availability statement

All data and R script used for the statistical analysis in this study is publicly available in the KNB repository: doi:10.5063/F19W0CXV.

Author credit statement

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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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chemosphere.2022.134279.

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