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"Non-traditional" stable isotopes applied to the study of trace metal contaminants in anthropized marine environments

Ferreira Araujo Daniel [1, *], Knoery Joel [1], Briant Nicolas [1], Vigier Nathalie [2], Ponzevera Emmanuel [1]

[1] Ifremer, RBE/CCEM, F-44000 Nantes, France
[2] Laboratoire d'Océanographie de Villefranche sur Mer (LOV), IMEV, CNRS, Sorbonne Université, France

* Corresponding author : Daniel Ferreira Araujo, email address : daniel.ferreira.araujo@ifremer.fr

Abstract :

The advent of Multicollector ICP-MS advent inaugurated the analysis of new metal isotope systems, the so-called "non-traditional" isotopes. They are now available tools to study geochemical and ecotoxicological aspects of marine metal contamination and hence, to push the frontiers of our knowledge. However, such applications are still in their infancy, and an accessible state-of-the-art describing main applications, obstacles, gaps, and directions for further development was missing from the literature. This paper fills this gap and aims to encourage the marine scientific community to explore the contributions of this newly available information for the fields of chemical risk assessment, biomonitoring, and trophic transfer of metal contaminants. In the current "Anthropocene" epoch, metal contamination will continue to threaten marine aquatic ecosystems, and "non-traditional" isotopes can be a valuable tool to detect human-induced changes across time-space involving metal contaminants, and their interaction with marine biota.

Graphical abstract

Highlights

► In the current “Anthropocene” epoch, trace metal contamination will threaten marine aquatic ecosystems. ► “Non-traditional” metal stable isotopes empower marine scientists to detect man-induced biogeochemical changes. ► They provide geochemical information about the sources and dispersion mechanisms of anthropogenic metals. ► They help understand bioaccumulation mechanisms, trophic transfers, and intracellular interactions. ► Marine scientific community can use this new isotope information for chemical risk assessment and biomonitoring.

Keywords : Marine pollution, Multi collector ICP-MS, Metal biogeochemistry, Isotope tracer, Metal stable isotopes

1. "Non-traditional" isotopes and their applications for the anthropized marine environments

The current Anthropocene epoch is characterized by humans' unprecedented exploitation of natural resources including metals, and consequently their release and ultimately the contamination of marine environments.[1–6] The inputs of trace metal contaminants in previously pristine environments is of great concern because these elements can damage health of humans and biota, disturb ecosystems, and compromise economical marine resources (fish and shellfish, algae, etc.).[7–15] Indeed, metal impacts may be amplified by their links to other major nutrient cycles, climate change, and other anthropogenic stressors.[16–18]

The advent of multi collector ICP-MS in the middle 1990's, accompanied by improvements in field sampling, chemical purification, automatization increased throughput, and allowed access to several "new" metal isotope systems (e.g., Li, Mg, Ca, Ti, V, Cr, Fe, Ni, Cu, Zn, Sr, Ag, Cd, Sn, Pt, Hg).[19–25] Still lacking a rigorous definition, these new systems are commonly referred to as "non-traditional" isotopes to distinguish them from both the non-metal (C, H, O, N and S) and radiogenic stable isotopes (Pb, Sm, Nd, Rb, Sr).[19–25] The latter have been studied for more than half a century,[26–29] and are routinely analyzed by isotope ratio mass spectrometry (IRMS) and thermal ionization mass spectrometry (TIMS), respectively.[25]

The availability of this (new) isotope information in biogeochemical modeling can help push the frontiers of knowledge on trace metal contaminants dynamics and their interactions with/within biota in the marine systems.[30] In this short overview article, we show that these so-called "non-traditional" metal stable isotopes can be used to obtain a more comprehensive view of metal contaminants in anthropized marine environments, covering (1) geochemically-oriented perspectives, focused on metal anthropogenic source apportionments across time and space combining natural archives and modern sampling devices; and (2) biology-flavored applications, linked to the bioaccumulation, trophic transfers and intracellular interactions of trace metal contaminants, up to physiological effects. The overview over these two complementary frameworks intends to call the scientific community's attention to the potential power of these new isotope tools to provide more accurate chemical risk assessments, and to develop more effective public policies related to metal pollution. We also indicate the main obstacles and possible directions for disseminating their use for studying anthropized marine environments.

2. A brief review about principles and nomenclatures

Isotopes are nuclides with the same number of protons, and therefore, belonging to same element, but with different numbers of neutrons, hence having different atomic masses.[31] The relative abundance of stable isotopes varies in nature because of isotope fractionation phenomena induced

in biogeochemical processes among reactants and products, phases, molecules, or compartments.[19,22] It results in an uneven distribution between light and heavy isotopes. This phenomenon is due to different chemical bond energies between isotopes of a certain element and a given ligand, and leads to a first-order linear correlation between isotope mass difference and isotope fractionation amplitude. Other processes like mass independent fractionation (MIF) processes occurring for instance in photochemical reactions (REF) may be observed for some metal isotope systems (e.g., Hg).[32–34] Isotope variations originated in these mass-dependent and independent mechanisms differ from radiogenic isotope systems (*e.g.* U, Pb, Th), for which isotope variations result from radioactive disintegration of parental nuclides to form daughter isotopes.[35–37] As convention, isotope ratios are expressed as the ratio between the heavy isotope over the light one (Table 1).[22] In general, the absolute ratio are rarely used for "non-traditional" isotope systems. Instead, they are typically reported as δ-values, which refer to the relative deviation of the isotope ratio of a given sample to an standard reference material (SRM), as follow:[22,38]

$$\delta\,(^{i/j}E) = \frac{R(\frac{^{i}E}{_{j}E})_{sample} - \quad R(\frac{^{i}E}{_{j}E})_{SRM}}{R(\frac{^{i}E}{_{j}E})_{SRM}}$$

where $R(\frac{^{i}E}{_{j}E})$ refers to isotope abundance ratio of the isotopes i and j of a given element (E).

3. "Non-traditional" metal stable isotope applied in biogeochemistry and ecotoxicology fields

3.1 Anthropogenic source apportionments and metal contamination mapping

Anthropogenic metallic materials, either the manufactured products themselves or their by-products, have *isotope signatures* inherited from the used raw materials and associated production processes (Fig. 1).[39–48] They often differ from the isotope compositions of non-anthropized metals present in water and sediments, whose isotope distribution is dominantly governed by natural weathering processes and biological activity activities across along the air-land-sea continuum (Fig. 1).[49–57] The distinction differences of isotope compositions between anthropogenic and naturally occurring metals enables is used to trace and quantify the portions of natural and anthropic sources by using mixing models (Fig. 2).[58–61] Metal isotope profiles of dated sediment cores are useful to verify anthropogenic contamination evolution across time (Fig. 2),[62–67] while surface sediments enable mapping the recent dispersion of metal contaminants.[59,68,69] Combining isotope ratios and geostatistical interpolation methods to model isotope variations across large space and time scales in the so-called "isoscapes" has been long used for non-metal stable isotopes (C, H, O, S) and radiogenic systems (Sr) for environmental, ecological, archeological and forensic purposes.[70–73] However, such applications remain rare for "non-traditional" isotopes probably due to expensive analytical costs and high time-

consuming sample preparation protocols.[74] A first attempt using Fe isotopes and dust deposition sampled along North Atlantic Cruiser modeled anthropogenic Fe dispersion in the global ocean (Fig. 2),[75,76] opening the road for similar studies focused on metal contaminants transfers in atmospheric and ocean interface.[77] While rapid improvements in the isotope characterization of sediment, seawater, and aerosols have occured,[78–83] analyses of particle-sized fractions of anthropogenic materials (e.g., road dust) and sediments, including colloidal, remain exploratory in marine studies.[84,85] Also, determining isotope compositions of specific labile metal speciation forms captured in *in*-situ sensors, such as in DGT (Diffusive Gradients in Thin-films) and PLM (Permeation Liquid membrane) is promising to study metal bioaccumulation by microorganisms and algae, even if potential artifacts associated with artificial isotope fractionation may hamper their use.[86] Preliminary experiments in controlled conditions with natural waters demonstrated the feasibility of using Zn isotopes measured in DGT passive samplers.[86] A subsequent DGT monitoring study proved its effectiveness for discerning discontinuous anthropogenic input into river waters.[87] In turn, controlled experimentations successfully applied the DMT (Donnan Membrane technique) to separate free and complexed metal ions bound to humic acids and estimate the isotope fractionation between these two species.[88,89] The applicability in the marine environment remain untested.

3.2 Marine biomonitoring anthropogenic inputs of metals

There is a great interest in using metal isotope information in biomonitor organisms to evaluate metal contamination status, since they are believed to act as proxies for the marine environment where they live and are easier to sample and characterize chemically. Over the world, and during the last 5 decades, bivalve mollusks have been used to establish geographical and temporal bioavailability tendencies of metals in the marine environment.[90–94] The availability of stored samples in environmental sample banks was instrumental in starting biomonitoring applications of the new isotope systems (Zn, Cu, and Li) have used these sentinel organisms.[58,95–99] Oysters record in their soft tissues the Zn isotope ratios of Zn bioaccumulated Zn from dissolved and particulate phases,[97,100,101] making it ideal for quantifying anthropogenic Zn bioaccumulation over time (Fig. 1).[58] As for Cu in bivalves,[102] the main difficulty is to verify the potential isotope fractionation during biological uptake and internal redistribution. It is believed that strong accumulators tend to have a low or insignificant isotope biological fractionation, because of their low excretion rates and hence, they tend to be more suitable for source tracking purposes.[103] Hg isotope characterization in fish predators from European coasts distinguished populations and related local Hg contaminant sources.[104] Alternative marine biomonitors of metal contaminants have yet to be explored.

3.3 Unraveling metal contaminant bioaccumulation mechanisms and trophic transfer

Dietary sources and metal speciation govern the entry of metals into marine organisms. From an ecological perspective, the trace metal accumulation pattern of a given metal at different trophic

levels will determine its biomagnification or biodilution of trace metals within trophic webs, and its related trophic isotope fractionation.[105,106] Constrains on Hg isotope fractionation factors involved in production and degradation of methylmercury (MeHg), the most toxic and bioamplified form of Hg, has allowed to use Hg isotopes to examine dietary sources and environmental controls on Hg speciation changes in MeHg in coastal marine systems.[32,33,106–109] Zn isotopes have also been useful to ascertain trophic levels and spatial variability on Zn dietary of marine mammals (Fig. 3).[110–112] However, most "non-traditional" isotopes remain unexplored in marine ecology of lower trophic levels, in part, due to uncertainties related to the time required to animal tissue to equilibrated with the diet.[113]

In an aquarium-based study, Li concentrations of mussel soft tissues increase as a function of water Li concentrations, but their Li isotope ratios ($^{7}Li/^{6}Li$) indicate a shift in their depuration mechanism above a certain concentration threshold.[114] Also, wild oysters and mussels show a remarkable difference in Cu isotope fractionation pattern linked to inter-specific physiological features.[102] Mussels display a particular enrichment in the heavy isotope due to homeostatic processes to regulate Cu at optimum concentrations (Fig. 3).[102] However, oysters show no such enrichment. Conversely, laboratory experimentation investigating Cd isotope fractionation at water-sediment interface demonstrated to be helpful to elucidate bioaccumulation routes (dissolved *vs.* particulate) in freshwater benthonic organisms.[115] Such approaches may help to characterize metal transfer from contamination sources, e.g., from legacies often found in benthic and sedimentary coastal systems.

Plankton does incorporates bioavailable trace metals in seawater and, being at the base of marine food chains, is an "inlet valve" for metal contaminants in upper marine trophic levels.[32,116–119] Anthropogenic metals are often under highly bioavailable forms that may imprint their specific isotope compositions into plankton. This can be used to trace the entry and propagation of metal contaminants through trophic levels.[77,120] Unfortunately, there is a lack of isotope studies in plankton samples collected in actual marine systems[121] and only few Hg,[122] Fe[123,124] and Zn[120] isotope experimentations in controlled conditions using specific culture species are available at present. Overall, these studies have demonstrated that the extent of the isotope fractionation in plankton uptake seems related to both the nature of the metal ligands, and to the specific strategy mechanisms (diffusion or complexation) involved in the transfer of metal ions from aqueous medium into living cells.[120] Hg isotope fractionation in phytoplankton of the euphotic zone of open ocean has given evidences of its own role in MeHg degradation in euphotic zone of open ocean.[122]

3.4 Metal isotope as biomarkers of physiological responses to metal contamination stress

Nearing the cellular level, cells regulate and activate tolerance mechanisms to maintain trace metal nutrients at optimum concentrations (homeostasis). They use organic ligands for uptake, storage and excretion of these metals, which may enhance their isotope fractionation.[125] The changes in the

patterns and magnitude of metal isotope fractionation in and by biological tissues as a response to metal level stress conditions can be used as biomarkers of metabolic disfunctions.[69,74] These innovative isotope biomarkers have been promising in botanic,[126] veterinary[127] and medical[74,128–132] applications for cancer and degenerative diseases.[132–134] Once transposed to the field of marine ecotoxicology, these similar approaches could verify if possible changes in isotope patterns of tissues or fluids (*e.g.*, blood) can indicate the physiological status of marine organisms. It would be expected that organisms' molecular responses to metal contamination, and causing disturbances on proteins and biomolecules network, DNA damages, or lipidic peroxidation, may induce a detectable isotope fractionation.[128] The production of reactive oxygen species (ROS) is one of the major mechanisms responsible for metal-induced toxicity.[135] These species may affect metal speciation in the inner cells of redox-sensitive trace metals and induce isotope fractionation that could be detected and used to pinpoint metal contamination as the source of the metabolic disturbances and environmental stress.[128,136] The quantitative tracking of metals in organisms may bring new light that could bridge an understanding between geochemists, familiarized with isotope applications, with ecotoxicologists familiar with physiology. In turn, ecotoxicologists can take advantage of common analytical techniques, sample preparation and theoretical isotope principles already developed in the medical research.

4. Perspectives and recommendations for future research

In the current Anthropocene epoch, metal contamination will likely continue to threaten the functioning of marine aquatic ecosystems. Here, we reviewed briefly diverse applications and recent advances of the "non-traditional" isotopes, and we showed how they can empower marine scientists to detect biogeochemical changes across time and space, and to investigate metal contaminant interactions with marine biota. Such applications are still in their early stages, and their growth still require improvements over the current state-of-the-art, in particular:

- To reduce analytical costs and high time-consuming sample preparation protocols by development of new analytical protocols, ideally greener (e.g., reagent consumption) and operating at higher throughput using e.g., automation;[137]
- To target particle fractions (according to their size, composition, origin etc…), including colloidal, for improving traceability of metal contaminants in aquatic systems and metal incorporation in organisms; to conduct laboratory experimentation to test integrating samplers' (e.g., DGT, PLM) suitability for isotope analysis; certainly, investigation of potential isotope bias related to filtration or accumulation of diffusive gradients remains necessary.[138,139]

- To extended biomonitoring concept to other sessile and mobile organisms (fishes, corals, benthos-dwellers) using e.g., multi-isotope fingerprinting would improve source metal discrimination;
- To quantify experimentally animal tissue isotopic turnover rate or isotopic half-life — up to now few studies have addressed this question;.[119,140]
- To constrain organotropism and related isotope fractionation; — since most studies concern only the Hg isotope systems;[68,141]
- To improve sampling and analytical protocols for planktonic trace metal analysis and their bioaccumulation mechanisms to reveal mechanisms of entry of metal contaminants in the base of trophic foow webs;
- To conduct ecotoxicology experiments using isotope metal cocktails to trace the genesis of biomarkers of their toxicity;
- To investigate the interactions between metal contaminant isotopes and new anthropogenic entities, such as micro-and nano-plastic particles[142] and other engineered nanomaterials.[143–145]

The expansion of applications using these isotope tools will undoubtedly benefit from the cooperation of scientists and of institutions involved in the study of marine pollution.

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Table 1. Summary of main "non-traditional" isotope systems and their respective δ-notations and standards reference materials (SRMs) conventionally used as δ-zero. Isotope-delta values are small numbers frequently presented in multiples of 10^{-3} or per mil (symbol ‰). In most literature, the denominator isotope is omitted, e.g., δ^{65}Cu instead $\delta^{65/63}$Cu. This last form constitutes the IUPAC recommendation.

Isotopes (abundance averages, %)	Preferred Isotope Ratio	δ-notation	SRM (δ-zero)
^{54}Fe (5.8), ^{56}Fe (91.8), ^{57}Fe (2.1), ^{58}Fe (0.3)	^{56}Fe/ ^{54}Fe	δ^{66}Fe	IRMM-014
^{58}Ni (68.1), ^{60}Ni (26.2), ^{61}Ni (1.1), ^{62}Ni (3.6), ^{64}Ni (0.9).	^{60}Ni, ^{58}Ni	δ^{60}Ni	NIST SRM 986
^{64}Zn (49.2), ^{66}Zn (27.7), ^{67}Zn (4.0), ^{68}Zn (18.4), ^{70}Zn (0.6).	^{66}Zn/ ^{67}Zn	δ^{66}Zn	IRMM-3702, IRMM- 651 JMC-LYON
^{63}Cu (69.2), ^{65}Cu (30.8).	^{65}Cu/^{63}Cu	δ^{65}Cu	NIST SRM 976 ERM -AE633 ERM- AE647
^{50}Cr (4.3), ^{52}Cr (83.8), ^{53}Cr (9.5), ^{54}Cr (2.4)	^{53}Cr/^{52}Cr	δ^{53}Cu	NIST SRM 979 NIST SRM 3112a IRMM-012 IRMM-625
^{106}Cd (1.25), ^{108}Cd (0.89), ^{110}Cd (12.49), ^{111}Cd (12.80), ^{112}Cd (24.13), ^{113}Cd (12.22), ^{114}Cd (28.73), ^{116}Cd (7.49)	^{114}Cd/^{110}Cd	δ^{114}Cu	NIST SRM 3108 BAM-I010 Cd-2211
^{196}Hg (0.1), ^{198}Hg (10.0), ^{199}Hg (16.9), ^{200}Hg (23.1), ^{201}Hg (13.2), ^{202}Hg (29.9), ^{204}Hg (6.9).	^{202}Hg/^{198}Hg ^{199}Hg/^{198}Hg	δ^{202}Hg (MDF) Δ^{199}Hg (MIF)	NRC NIMS-1 NIST SRM 3133 NIST SRM 2225 NIST SRM 1641
^{7}Li (92.4), ^{6}Li (7.6)	^{7}Li/^{6}Li	δ^{7}Li	NIST RM 8545
^{107}Ag (51.8), ^{109}Ag (48.2)	^{109}Ag/^{107}Ag	δ^{109}Ag	NIST SRM 978a

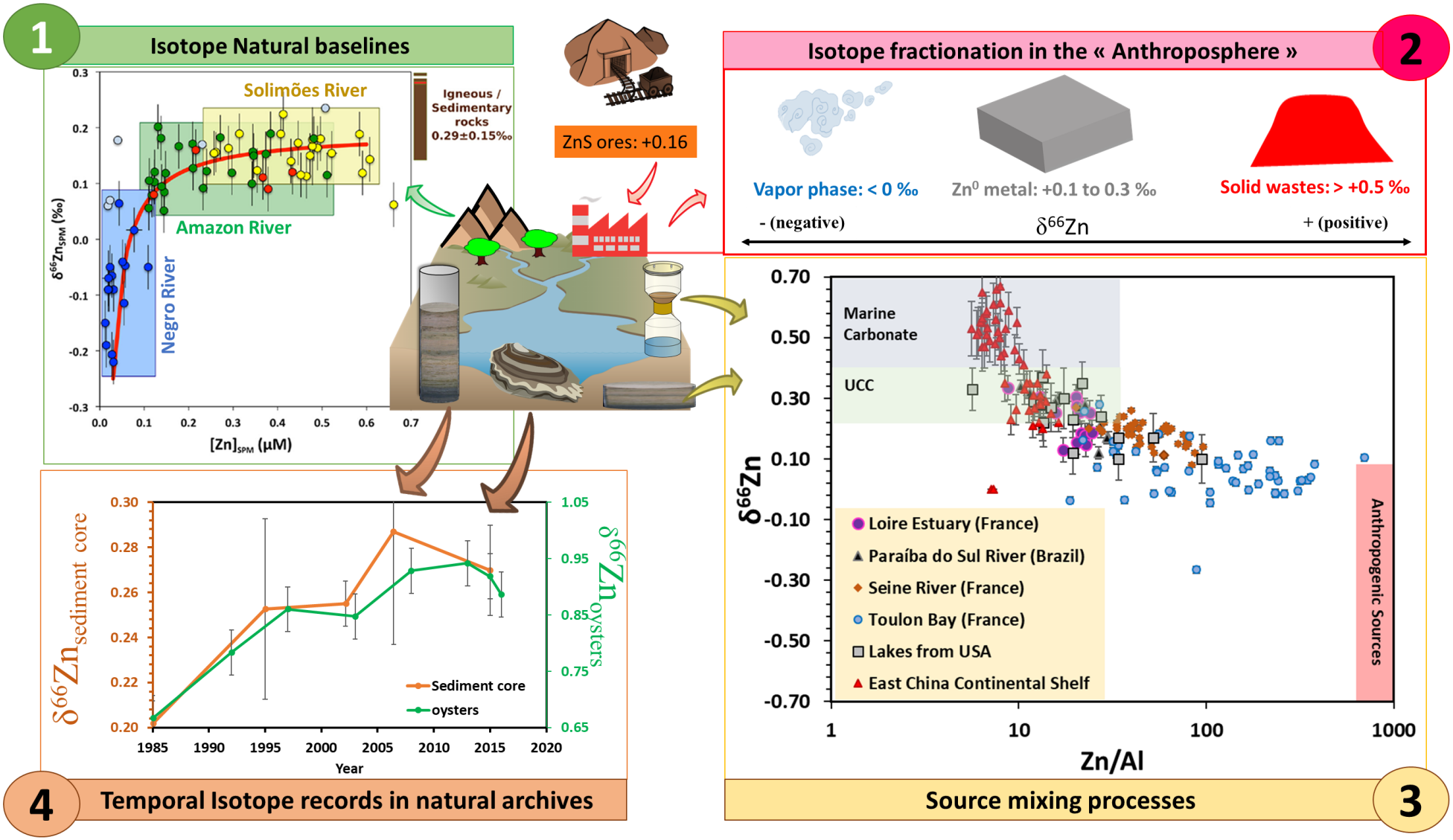

Fig. 1. Illustrating contaminant tracking principles with Zn isotopes. **1**-Watershed geology settings, weathering and primary activity determine the specific natural isotope baselines for a given systems aquatic, like fluvial-estuarine ones[53]; **2**- In the "Anthroposphere", ore refining and other industrial processes stan isotope signatures in anthropogenic materials distinguishable from the natural background;[146] **3**- source mixing processes reflect the balance between these sources;[49] and **4**-its historical evolution is recorded in natural archives, including sediment cores and biomonitoring organisms, like oysters[58].

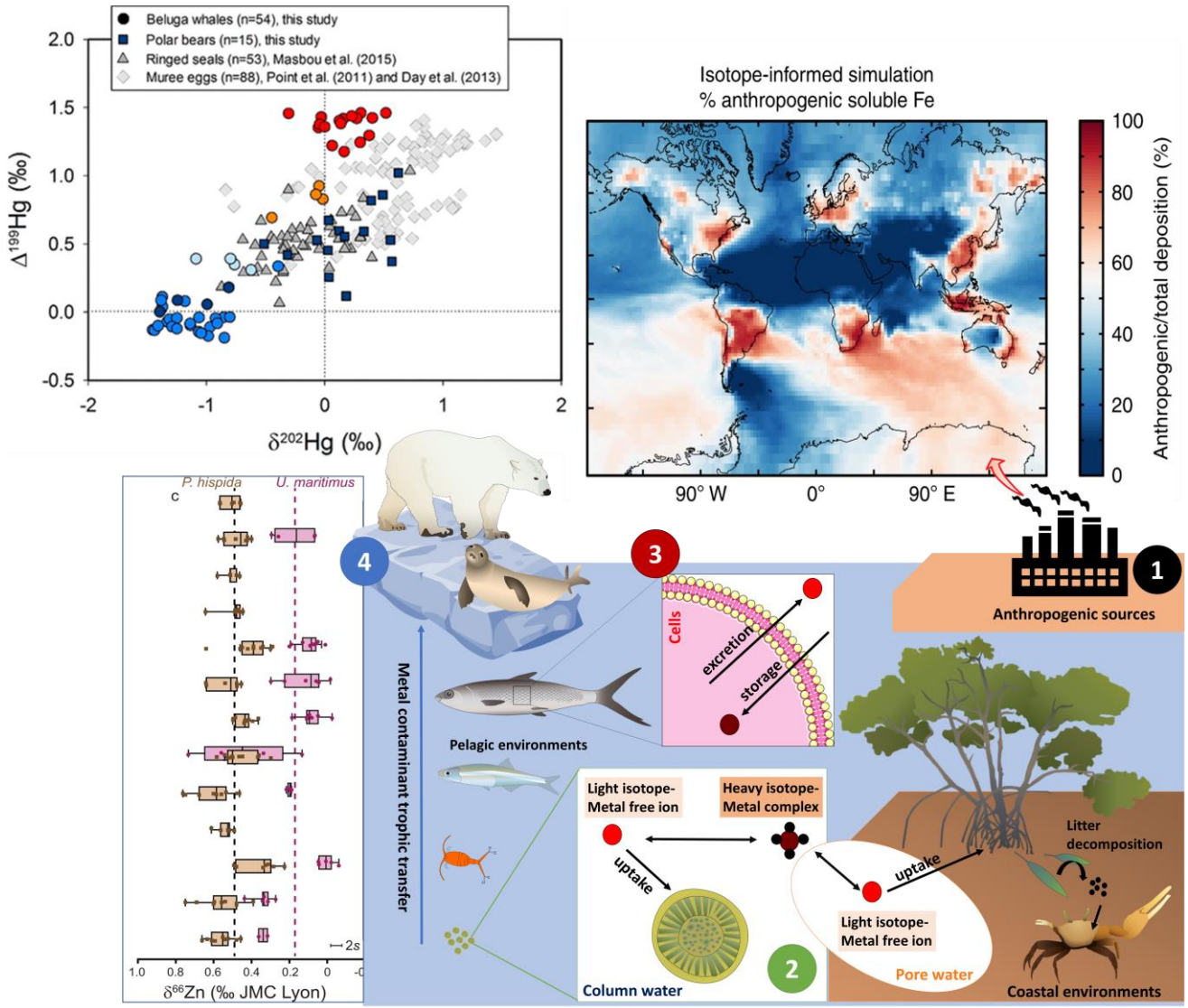

Fig. 2. Investigations on anthropogenic metal entries and their transfer to trophic chains in the marine environment using "non-traditional" isotopes. **1-** Isotope modeling of anthropogenic metal dispersion in the ocean (the case for Fe);[75] **2-** Isotope fractionation between metal free ion and metal complex forms and subsequent biological uptake by phytoplankton[120] and mangrove trees[69]; **3-** Biological fractionation involved in metal cellular trafficking;[147–149] **4-** Zn[112] and Hg[150] isotope fractionation in marine top predators of Artic marine mammals. For Hg, MDF *vs.* MIF plots in marine animals reveal geographic isotopic differences related to different dominant Hg biogeochemical processes occurring across the space.[32] Black one- and two-sided arrows indicate equilibrium and unidirectional isotope fractionation processes, respectively.

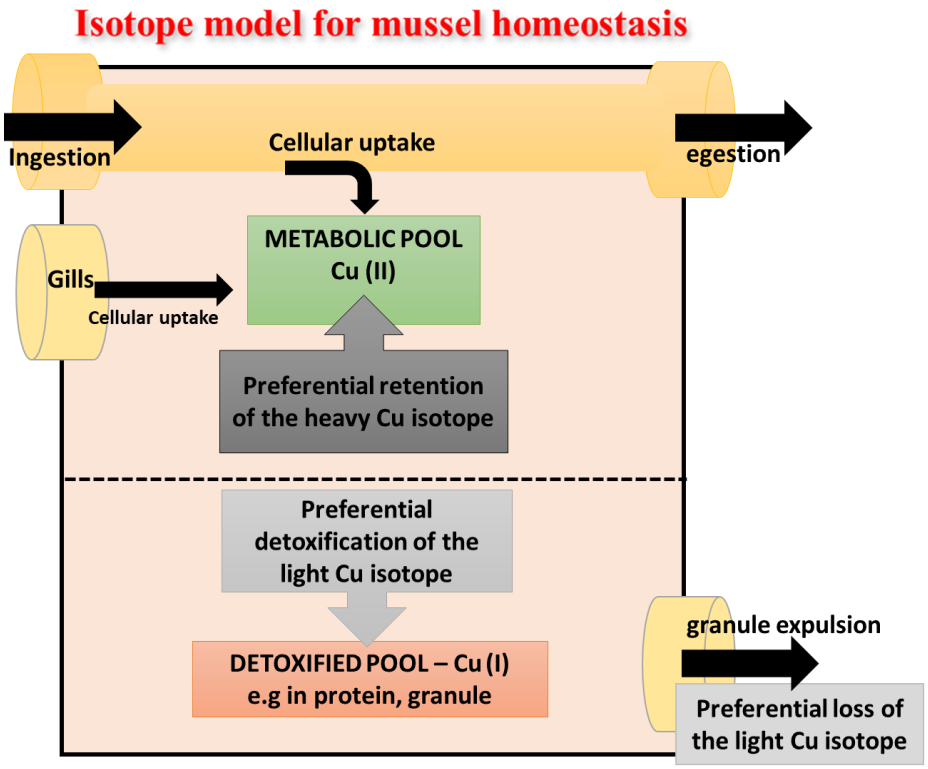

Fig. 3. A conceptual scheme of Cu isotope fractionation in the homeostatic regulation of the mussel *Mytilus edulis* based on previous studies.[102] After incorporation of Cu via particulate and dissolved phases by stomach and gills, respectively, Cu is partitioned into two components — metabolically available metal and stored detoxified metal. This partition, accompanied by redox processes, leads to an isotope fractionation between these two pools: a "metabolic pool" associated with the Cu (II) form and enriched in the heavy isotope; and a "detoxified pool" where reduced Cu (I) is dominant and there is preferential stocking of the light isotope. The elimination of the detoxified Cu pool results in a net balance isotopically heavy for mussels' tissues.