Understanding the impact of chemicals on marine fish populations: the need for an integrative approach involving population and disease ecology
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Abstract
The impact of acute and chronic marine pollution on the population changes of individual fish remains mostly unknown. In this paper, we share our study and review similar published work, emphasising fish health monitoring in European Seas and illustrating it using case studies. Arguably, an integrative approach is needed to assess the impact on population of chemical contaminants, beginning with field observations and complemented with experimental (laboratory and mesocosm) studies and modelling. Field surveys and monitoring using fish biomarkers should be intensified and ideally integrated with population statistics and fish ecology knowledge. Moreover, the indirect effects of chemicals — altering ecosystem functions — and the monitoring of immunological biomarkers and fatal diseases in wild fish populations should receive more attention.

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Introduction
Although the negative and positive effects of contaminant sources on marine fish abundance and species richness have been observed in local populations in susceptible areas (coral reefs, rocky bottoms and vegetated habitats), these contaminants have been suggested to not majorly impact fish diversity [1]. However, the sublethal effects of known chemicals on the biology of marine fish species have been well documented [2–6], although these cannot be easily translated into wild population—level effects [7, 8**]. To link direct molecular initiating events with adverse outcomes, adverse outcome pathways have been proposed as a new paradigm [9]. Considering real-world complexity, amid many stressors, wild fish populations cope with complex chemical mixtures during their life cycles. Indeed, scaling up from the effects of low levels of chemicals from individuals to changes at the population level and verifying if these can impact the sustainability of wild fish populations is quite challenging. Years of monitoring is required to determine if a natural fluctuation in population size becomes a significant decline. Furthermore, the potential impact of chemicals on marine fish populations may be quite hard to detect amid the changes imposed by other stressors (e.g. fishing practices and climate change) [10*, 11]. Here, we review the chemical impact on marine fish health, emphasising European studies and describe our experiences and opinions of linking such impacts with population-relevant end points. Although emerging contaminants such as micro-plastics/nanoplastics and nanoparticles could be relevant, they have been excluded from the review.

Fish biomarkers in marine monitoring and assessment
Environmental coexposure to a wide variety of chemicals may cause sublethal effects on marine and estuarine fish species, the effects ranging from cellular, biochemical, histological and behavioural alterations to subtle impacts on reproduction and normal endocrine and immune functions [6,12–15]. The contaminant-related effects are notably found not only in fish from polluted estuaries, coastal waters and saltwater lagoons but also in offshore and deep-sea species, especially those associated with sediments and production water or in those occupying higher trophic levels [6,14,16–22].

Measuring sublethal and organisinal toxic responses in wild fish can not only provide integrated temporal and
spatial information about contaminant exposure and effects but also indicate acute pollution events [23–26]. Fish biomarkers as such are biologically more meaningful than mere measurements of chemical body residues [2,22,23]. They have, over time, led to the development and successful implementation of fish biomonitoring programs or epidemiological surveys in European seas and elsewhere [6,17,20,24,27–30]. In this work, variable combinations of core biomarkers of chemical exposure and effects have been applied, with (partial) coverage of major adverse outcome pathways and ecological endpoints, including genotoxicity, neurotoxicity, endocrine disruption, histopathology, diseases and reproductive success [27]. Noticeably, to date, immunological biomarkers to evaluate the potential immunotoxic effects of contaminants are rarely considered in biomonitoring [31**]. However, contaminants are found to modulate the innate immune system of marine fish and increase pathogen susceptibility, influencing the organism’s fitness and survival, causing the prevalence and spread of diseases and parasites in populations [31**]. Hence, the fish’s immune system, as a target of environmental contaminants and consequent biomarker development, deserves more attention.

The routine monitoring of fish biomarkers or fish health in Europe started in the mid-1980s. So far, the stored and validated data in national and regional convention data banks (i.e., the International Council for the Exploration of the Sea/Convention for the Protection of the Marine Environment of the North-East Atlantic (ICES/OSPAR), the Baltic Marine Environment Protection Commission (HELCOM) and the Mediterranean Pollution Monitoring and Research Programme (MED POL)) have been from a handful of pelagic and demersal fish species, providing incomplete coverage of European sea basins. Notably, the long-term data sets on well-established fish exposure biomarkers ethoxyresorufin-O-deethylase, polycyclic aromatic hydrocarbon (PAH) metabolites and fish diseases (externally visible diseases and parasites, macroscopic liver tumours/neoplasms) are unique and of great value for marine quality assessment [33–37*]. More recently, fish tissue chemistry, exposure and effect biomarkers have been implemented in holistic chemical biomonitoring frameworks to assess and protect the health of Europe’s marine ecosystems [14,18,20,28,38]. In addition to regulatory drivers (EU Marine Strategy Framework Directive) and developing new technologies [39], visible impacts of large oil spills, frequent reports of fish with unsightly ulcers and tumours in the 1980s and 1990s and the discovery, during the turn of the century, of oestrogen-induced feminisation in fish (intersex gonads) were important drivers of marine fish biomonitoring [5,16,29,40]. In Europe, expert groups under the auspices of ICES and Regional Sea Conventions, national monitoring activities and a series of international sea-going workshops were instrumental in this process [23]. Unfortunately, largely owing to political and budget constraints, fish biomonitoring in Europe has been in decline, threatening future assessments.

**Major challenges**

Acute and often visible fish mass mortalities caused by oil spills, chemical incidents or harmful algal blooms are often clear-cut cases [41–43*], but mid- and long-term effects of chronic chemical exposure on fish stocks or local populations remain largely unclear [44–47*]. Our research on fish populations after the Prestige oil spill in 2002 in the NW Spanish coast is an example [48]. In 2003, exposure biomarkers related to petroleum hydrocarbon compounds were found induced in two benthic fish species, four-spot megrim (*Lepidorhombus bosci*) and dragonet (*Callionymus lyra*) and, two and three years after, declined to background levels [49]. Although decreased fish species abundance was also observed in 2003, it cannot be exclusively linked to the spillage [50]. Reference points of the stock assessment of the four-spot megrim invalidated the hypothesis of an increase in mortality due to the spill, the most plausible explanation being a problem of gear accessibility to the species in 2003 [51]. Overall, the closing of the fishing season, declared after the accident, had likely reduced the fishing mortality, contributing to population dynamics.

In the 1980s, the European flounder (*Platichthys flesus*) in the Dutch Wadden Sea near drainage sluices of Lake IJssel showed epizootics of skin ulcers with associated mortality, possibly due to a combination of salinity stress, nutritional deficiencies, high bacterial loads and obstacles to fish migration by the sluices, but no indication of chemicals was implicated [52]. Yet follow-up surveys revealed a significant association between ulcer occurrence and measured body burdens, PAH metabolites and toxicopathic liver lesions [52]. These extended investigations helped us to understand that in addition to osmotic stress and pathogen pressure, chemical stress and changing contaminant bioavailability through chemical-induced immunosuppression likely contributed to the observed ulcer epizootics. Owing to the locally high fishing pressure, possible population impacts remained obscured [52].

Singling out chemical stressors from alternate anthropogenic (i.e. fishery practices and habitat alterations) and environmental stressors (i.e. pathogen pressure, changing climate, eutrophication and osmotic stress), which can also impact the health of individuals and the integrity of ecological processes, is often not possible [23,29,48,53–55]. Hypoxia and eutrophication of marine waters have been increasing globally. In addition to impairing basic physiological functions and altering fish behaviour, chronic and seasonal hypoxia cause endocrine disruption and reproductive impairment in estuarine fish populations [56,57]. Finally, biotoxins linked to algal blooms and jellyfish invasions are found to adversely
affect fish health, inducing gill pathologies, increasing susceptibility to diseases and reducing growth and survival [43*,58,59].

Although pollution is one of the least studied stressors in marine ecology, it is plausible that the indirect chemical effects on fish populations (owing to altered ecosystem functions) are more relevant than direct effects [60].

**In search of causal associations**

The chemical impact on wild fish populations can be demonstrated by monitoring some of the structural or dynamic characteristics of the population, preferably in parallel to chemical biomonitoring, and finding them altered. The biomass assessment of fish stocks often involves costly fishery surveys, and its estimation is usually performed using fishing gear, which can be considered as being selective, influencing stock size estimates [61]. Newly developed methods could bridge the gap between chemical-related effects and population changes and establish possible causal associations. Stock assessment surveys are usually conducted across wide geographical areas comprising different degrees of environmental contamination. The recent development of Bayesian modelling and inferences in fishery research [62] enable the detection of unusual temporal patterns in fisheries time-series data, in particular, in subareas where local fish populations respond differently to anthropogenic drivers (i.e. chemical exposure) [63]. On the other hand, the development of genetic analyses might prove to be a new and useful approach to noninvasive monitoring of fish stocks in the future [64**]. Fish chemical and biomonitoring programs could benefit from it, incorporating measurements, that is, of environmental DNA in seawater from the same location where the catch was performed and obtaining supplementary information on, for example, migratory patterns or biomass of key fish species.

Nevertheless, monitoring fish population—relevant end points (e.g. fitness, growth and fecundity) is the first critical step in investigating the association with the levels of exposure, tissue burden and contaminant-biomarker responses. However, the currently practiced effect biomarkers do not easily translate to such end points, thus constraining the assessment of impacts on wild fish populations [6,7]. Causal studies based on surveys or biomonitoring data are further constrained as the final insights show statistical associations between chemicals and other stressors and biotic variables rather than proven causation. Other processes such as chemical bioavailability, chemical tolerance, disease susceptibility, metabolisation and fish migration patterns might further constrain field assessments, and consequently, the absence of a direct relationship between environmental pollution or elevated body burdens and fish health effects is frequently reported. The red mullet (**Mullus barbatus**) population from chronically polluted areas along the Spanish coast is an example. The species showed elevated responses of certain contaminant-related biomarkers (i.e. **ethoxyresorufin-O-deethylation** activity) and high concentrations of contaminants, surpassing, in some cases, the environmental threshold values established for fish (i.e. certain polychlorinated biphenyls) [18] (PE Crespo., final degree work, Polytechnic University of Cartagena, 2016). Although some local populations have been shown to exhibit suboptimal health status (low fitness and gonadosomatic indexes), the contaminant body burden only partly corresponded to sedimentary chemistry [18,65]. Furthermore, the Spanish Mediterranean stock of this species displayed a stable trend during 2006—2015, showing no overall indication of any chemical impact (AS Rehab Farouk, final degree work, University of Alicante, 2017). Another example refers to the bottom-dwelling flounder in the North Sea [34]. The prevalence of chronic liver neoplasia in this flatfish does not correlate with sedimentary PAH levels [34]. Yet the implication of genotoxic/carcinogenic PAHs in disease development in this species was convincingly shown in a mesocosm study [66]. This discrepancy may be due to the migratory behaviour of the species, resulting in differential exposure to contaminant concentrations during various life stages. Thus, although tumour-initiating compounds such as PAHs are a necessary cause, the ultimate distribution patterns of liver neoplasms in North Sea flounder populations seemed primarily determined by a combination of tumour-promoting risk factors, which may be chemical or nonchemical [34]. Marked seasonal cycles in energy reserves could make such migratory species particularly vulnerable to the effects of persistent contaminants (i.e. dioxins, polychlorinated biphenyls) that could act as tumour promoters [67].

**Towards an integrative approach involving population and disease ecology**

Applying suborganism- or organism-level biomarkers to a fish population does not make them fish population—level biomarkers because fish population responses are not sums of organismal responses. It is recognised that growth, survival, reproduction and movement rates in fish populations change in response to variation in population density (or numbers), termed ‘density-dependent compensatory responses.’ However, if density-independent effects such as those caused by chemical pollution are dominant or exceed the limits of ‘compensatory responses’ of the population growth, changes in mortality or fecundity will affect population abundance [7,68].

In general, to affect population dynamics, mass mortality events, frequently associated with outbreaks of infectious diseases [69], have to affect a large percentage of individuals of the same population in a short period. Long-term analyses of major skin diseases and parasites...
in North Sea fish have suggested, among other factors, that chemical-induced immune suppression may influence the observed temporal changes of disease prevalence [22,34,36*]. Such end points are useful general indicators of environmental quality, owing to their nonlethal course. If immunotoxic chemicals lead to the outbreak of fatal infectious marine fish diseases, for example, viral nervous necrosis [70], it is much harder to prove, and therefore perhaps mostly unknown, but evidently most relevant to population impacts and loss of biodiversity [68–71]. Therefore, this area demands more research, involving both population and disease statistics, and modelling approaches. On the other hand, it is widely demonstrated that the developing fish embryo or larva is the most sensitive stage in the life cycle of a teleost [72]. Furthermore, floating eggs, embryos and larvae may be particularly exposed to high levels of contaminants in the sea-surface microlayer [73]. However, field assessments of biological effects in early developmental stages due to chronic exposures to chemicals and their impact on fish population dynamics are very limited and seriously understudied [41,46,54,74].

Ideally, the causal evidence of contaminant effects in fish should be based on a weight of evidence approach using epidemiologically based field surveys and experimental studies on field-collected material [26,67,75,76]. Combined approaches using integrated field studies, controlled laboratory exposures and semifield studies (e.g. mesocosm or caging experiments) are most useful [67,76]. The framework of Bradford Hill criteria for causation has successfully been applied in several marine fish epidemiological studies [67–77]. However, in some cases, these criteria are not fulfilled: some biological responses that act via an endocrine mode of action occur at low or very low contaminant concentrations in early life stages, the effects being apparent much later in life [8**]. Therefore, in this case, the likelihood of establishing a causal link between observed effects in marine fish and chemical contaminants from any source is quite low, demanding extremely long-term data sets. Applying expert systems in biomonitoring for the prognosis of impacts and diagnosis of causes have been noted in the past and might be worth revisiting [30]. Furthermore, mathematical models to assess the impact of contamination on fish population dynamics should be further explored [78,79].

Recently, in polluted areas, some wild fish were found to have adapted responses and increased tolerance to contaminants over time [80,81*]. However, whether fishes adapted to one pollutant are better or less able to cope with other pollutants or stressors in a changing environment remains uncertain [81*]. Such population-level factors could potentially confound epidemiological surveys or biomonitoring results and should be considered in ecological risk assessment processes [81*]. Finally, monitoring fatal diseases of fish species (commercial) should be focused on. The marked absence of immunological biomarkers in fish biomonitoring should be considered a key weakness because they are essential in assessing the immunocompetence of fish before disease outbreaks [29,31**,67]. Their development and implementation should be prioritised.

Conclusions and outlook

While marine fish biomonitoring, combined with chemical and physical measurements where possible, is useful for conservation purposes, it could gain immense value by relating the results to changes in fish populations.

To advance our knowledge of the topic’s complex multifactorial nature, a more integrative approach is proposed, one that will incorporate chemical biomonitoring and population or stock assessment surveys, complemented with experimentation (laboratory and mesocosm or cages) and modelling approaches. Ideally, information from fish chemical biomonitoring would be combined with data from fish stock assessment and disease surveys. Moreover, the effects of chemicals on offspring and, in particular, the fish’s immune status and further understanding of the ecology of its diseases should be emphasised.

Finally, the acute and chronic exposures to chemicals should be placed in perspective with other environmental threats to marine fish populations, such as global warming, oxygen deficiencies and biotoxin events.

Conflict of interest statement

Nothing declared.

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Using ICES/OSPAR criteria and a combined assessment of three disease categories, the authors demonstrate that health effects classified as unacceptable were rare and mainly affected dab from the North Sea.


This publication contains a long-term data sets of great value on well-established fish exposure biomarkers (EROD, PAH metabolites) and fish diseases (externally visible diseases and parasites, macroscopic liver tumours/neoplasms).


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In this review, authors present novel data showing that variants of the CYP1A gene have been under selection in fish living in heavily polluted waters with crude oil and discuss the potential costs associated with these adaptations on fitness in unpolluted water conditions.