



## Micro- and nanoplastics effects in a multiple stressed marine environment

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### ABSTRACT

Micro- and nanoplastics (MNPs) pollution is an environmental issue of concern, but current effect assessments often overlook realistic scenarios, and a contextualised vision of the magnitude of the impact of complex mixtures of MNPs together with other environmental stressors is urgently needed. Plastic particles exist in the environment as complex mixtures of particles from various size ranges, shapes, and polymer types, but the potential effects of realistic MNPs mixtures and concentrations are still poorly understood, and current effects data is insufficient to produce high quality risk assessments. Organisms exposed to MNPs in the marine environment are simultaneously subjected to global change driven stressors, amongst others, such as ocean warming (OW), marine heat waves (MHW), ocean acidification (OA), and ocean deoxygenation (OD). Stress responses due to MNPs ingestion can, in particular cases, lead to a metabolic and energetic cost, which may be aggravated in the case of organisms already vulnerable due to simultaneous exposure to global change-related stressors. In this work, we discuss how MNPs effects could be assessed while considering plastics complexity and other environmental stressors. We identify knowledge gaps in MNPs assessments, acknowledge the importance of environmental data acquisition and availability for improved assessments, and consider how mechanistic ecological models can be used to unveil and to increase our understanding of MNPs effects on marine ecosystems. Understanding the importance of plastic pollution in the context of other stressors such as climate change and their potential combined effects on marine ecosystems is important. The assessment of realistic effects of MNPs on all biological levels of organisation should consider the co-occurrence in the environment of global change-related stressors. Even though the number of studies is still limited, recent effect assessment reports indicate that the MNPs interaction with global change stressors can affect processes in organisms such as ingestion and digestion, energy allocation, growth, and fecundity. The potential impact of this interaction at population levels is largely unknown and requires increased attention from the research community, to provide information to stakeholders on the vulnerability of marine species and ecosystems now and under future environmental conditions.

### Introduction

Micro- and nanoplastics (MNPs) pollution is an environmental issue of concern (Catarino et al., 2021), but current effect assessments overlook realistic scenarios, such as exposure concentrations, complexity of polymer types, shapes and weathering stages, and contextualisation with other environmental stressors (Bucci et al., 2020; Koelmans et al., 2022b; Rochman et al., 2019). Plastic items enter the environment, either because of accidental loss or poor waste management practices, and can be transported to marine environments via land runoff, water bodies, wind, or currents (Schwarz et al., 2019). Once in the environment, plastic debris undergo physico-chemical stress (e.g., abrasion, UV radiation), which leads to monomers and additives leaching from the polymer matrix (Khan et al., 2021; Koelmans et al., 2014), and to the fragmentation of larger items (Kalogerakis et al., 2017; ter Halle et al.,

2016) to micrometric (microplastics, MPs, 1 - 5000  $\mu\text{m}$ ) and nanometric (nanoplastics, NPs, < 1000 nm) size ranges (Koelmans et al., 2022b). In addition, industrial beads and pellets, produced intentionally as polymeric MPs or NPs, and used in applications such as in personal care products, paints, scrubbers, can also be unintentionally release into the environment (SAPEA, 2019). Environmental MPs are therefore composed of a myriad of shapes, sizes, densities, and weathering states (Koelmans et al., 2020; Kooi et al., 2021; Rochman et al., 2019). Even though the identification and quantification of environmental NPs represents an extreme technological challenge, there have been reports of NPs observed in the environment (Materić et al., 2020), and their presence may add to the complexity of MP mixtures. Based on current reports for environmental samples of MPs, estimated concentrations of MNPs in seawater are less than 1  $\mu\text{g}$  of MNPs / L [ $10^{-6}$  -  $10^9$  MNPs / L (Lenz et al., 2016);  $10^{-1}$  MPs / L (median) (Bucci et al., 2020)], but only few studies have assessed effects at environmental relevant levels of MNPs. Furthermore, MNPs are considered as complex mixtures (Koelmans et al., 2022b; Rochman et al., 2019) that can interact over

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time with organisms, at scales that go from molecular to ecosystem levels of biological organisation, and in combination with other existing environmental stressors, such as climate change. Plastic waste, including MNPs, is omnipresent and persistent in marine ecosystems (Lehner et al., 2019), and can be observed in the marine environment at concentrations that exceed safety thresholds (Everaert et al., 2018). The complexity of mixtures of MNPs, and their interaction with other major environmental stressors, is currently a major challenge that requires consideration and that is faced by researchers in the plastic pollution field, conservationists, managers, and policymakers.

In the environment, organisms exposed to MNPs are also subjected to a multitude of environmental stressors, particularly to those related to increased anthropogenic emissions of atmospheric greenhouse gases and climate change, such as ocean warming (OW), marine heat waves (MHW), ocean acidification (OA), and ocean deoxygenation (OD) (Cooley et al., 2022). Current projections indicate that the anthropogenic CO<sub>2</sub> accumulation in the atmosphere and oceans will induce by 2100 a 3 °C rise in the mean sea surface temperature, a pH decrease of 0.3 units (IPCC “business-as-usual” projection RCP8.5 of no reduction of greenhouse gas emissions) (Bindoff et al., 2019) and up to 7% reduction in the average ocean oxygen concentration (Keeling et al., 2010). Additionally, led by OW, stratification and eutrophication, hypoxic zones (< 2 mg O<sub>2</sub> / L) (Vaquer-Sunyer and Duarte, 2008) are expected to increase in frequency and extent, particularly in estuaries and shallow tidal areas (Bindoff et al., 2019). In coastal environments, the frequency, extent, and magnitude of MHW is expected to increase with a global warming beyond the 1.5 °C projection threshold (Pörtner et al., 2022). By 2100, the fraction of the oceans’ surface layer (0 - 5 m) at risk due to MPs will increase up to 1.62%, with hotspot areas in semi-enclosed seas, e.g., Mediterranean Sea and Yellow Sea (Everaert et al., 2020), with predicted concentrations of NPs estimated to be higher than those of environmental MPs (Lenz et al., 2016). Projected future scenarios for all global change driven stressors may, with a high degree of certainty, lead to major impacts on the biodiversity and functioning of the marine environment (Cooley et al., 2022). Nonetheless, the major challenge in predicting MNPs and climate change-related effects relies in the fact that combined effects of environmental stressors cannot be linearly derived from each single effect (Pirota et al., 2022), but only recently have the first studies on MNPs effects in a multiple stressor context been published. For example, on a bibliographic search on the Scopus (Elsevier, 1st September 2021, see supplementary information) of peer-reviewed articles published between 2010 and 2020, the cumulative number of studies, concerning the marine environment, on research related to global change was of 12,368, while for MNPs impacts/effects was 1720 (Fig. 1, Supplementary Table S2). In the same bibliographic search, when we combined terms related to global change and MNPs research, the number of peer-reviewed studies returned was limited to 25, with half of which (12) published in 2020 (Fig. 1, Supplementary Table S2). In this work, we discuss how MNPs effects could be assessed accounting for plastics complexity and other environmental stressors, we identify knowledge gaps in MNPs effects assessments, we acknowledge the importance of environmental data acquisition and availability and consider how modelling effects can increase our understanding of MNPs effects on marine ecosystems in a multiple-stressor context.

### Quantitative assessment of MNPs effects as complex stressors in a changing environment

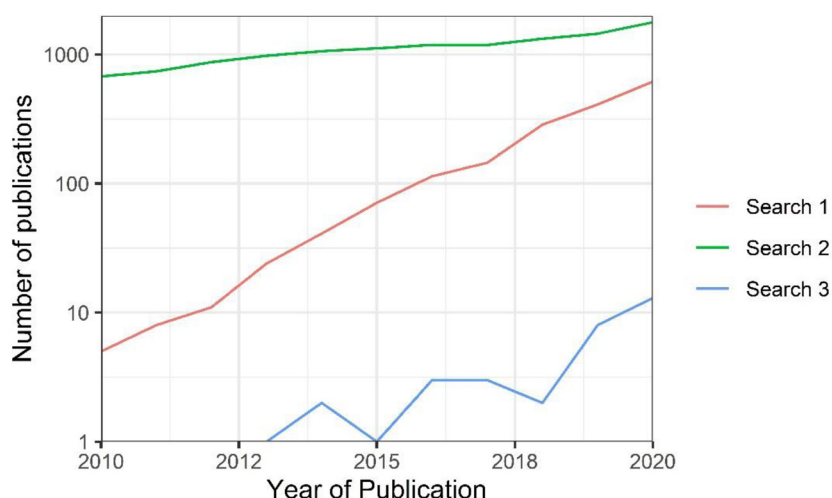
Assessing the biological responses to multiple stressors’ exposure, in particular the combined effects of MNPs mixtures and global change, requires an array of approaches, from laboratory and field-based experimental work to environmental observations, and the development of mechanistic and empirical models (Cooley et al., 2022; Pirota et al., 2022). Plastic particles can lead to stress responses that generate a cascade of internal changes within a system, out of its operating range (ac-

ording to the stressor definition by Van Straalen, 2003 and Segner et al., 2014), which lead to stress responses that can have a potential high metabolic and energetic cost (Galloway and Lewis, 2016). Pirota et al., 2022 have suggested a conceptual framework to estimate combined responses of a biological system to multiple stressors exposure, which encompasses a spectrum of analysis and methodologies between a purely data-driven approach (phenomenological) and a process-driven approach (mechanistic). Pirota et al., 2022 assumes that when data is available from a range of stressor doses, the combined effects of stressors can be described empirically with a very low bias, but combined effects can only be described or predicted along the observed range of stressor doses. On a first stage, experimental work exposing a biological system should be conducted using single stressors to provide background information, which will subsequently enable the design of multiple-stressor exposures with increased complexity and methodological challenges (Boyd et al., 2019; Griffen et al., 2016). Preliminary studies can further assist in the interpretation of the observed effects, for instance when interactions between stressors are not linear (Boyd et al., 2019; Griffen et al., 2016).

In multiple stressors assessments, the number of treatments often limits the design of a fully factorial experimental approach. For example, assessing the responses to an increasing number of levels for each tested stressor becomes highly complex in orthogonal experimental designs when the number of stressors is above two (Griffen et al., 2016), making the manipulation of an increased number of levels for each stressor technically challenging and infrastructure demanding (Boyd et al., 2019, 2018). At community level, the total stressor intensity, i.e., the combined stressor effect experienced by all the present species, is further dependant not only of the number of stressors involved in the experimental design, but also on the selected dose/exposure level (Holmes et al., 2021). To address such challenging designs, researchers can use a stepwise approach by combining a suite of simpler experiments following best practices to guarantee enough statistical power to identify impacts (Boyd et al., 2019). For example, fully factorial designs can be simplified using fractional factorial designs (Gunst and Mason, 2009), or by using collapsed designs where a dominant stressor, i.e., a factor, is identified and other stressors are grouped together into combined factors (Boyd et al., 2018, 2016). Ultimately, any experimental design should be adequate to answer the scientific question proposed, while considering environmental relevant levels in terms of projected environmental shifts (Boyd et al., 2018). In the case of MNPs, the current knowledge of single pristine particle types and in isolation from other environmental stressors are key building blocks of knowledge that can now enable the design of elaborated effects assessments.

### Microplastics as complex stressors

Microplastics are complex stressors in the marine environment, but the potential effects of realistic MPs mixtures and concentrations is still poorly understood. Because biota are mostly exposed to MPs via ingestion, reported effects are associated with inhibition of digestive processes (Blarer and Burkhardt-Holm, 2016), or induction of a false sensation of satiation that results in malnutrition and hunger (Guilhermino et al., 2018). Reports suggest that MPs could potentially increase of the bioaccessibility via ingestion of toxicants associated with the surface or matrix of plastic polymers (Khan et al., 2021), but co-contaminant bioaccessibility is considered negligible when compared to other food sources (Diepens and Koelmans, 2018; Khan et al., 2021; Koelmans et al., 2022a). Microplastics, particularly in the case of fibres, can be retained in the gut of organisms for long periods of time (Grigorakis et al., 2017) and have been reported in both wild specimens (Welden and Cowie, 2016) and laboratory assessed organisms (Romanó de Orte et al., 2019). The effects of MPs on marine organisms that are primarily linked to a reduction in food consumption, can impact growth, survival, and reproduction, and have a major incidence in primary consumers, such as zooplankton and other small in-



**Fig. 1.** Number of published peer-reviewed research papers on global change and MNP research in the marine environment in each year [Y axis in logarithmic scale ( $\log_{10}(N+1)$ ), between 2010 and 2020. Bibliographic searches, done in separate using Scopus.com (Elsevier) on 1st September 2021, refer to the marine environment, specifically to micro- and nanoplastics (MNPs) research [Search 1, total of 1720 results], global change research (including global warming and ocean acidification) [Search 2, total of 12,368 results] and combined MNPs-global change research [Search 3, total of 25 results] (Supplementary Table S2). Methodology and terms used in the bibliographic searches (Supplementary Table S1) are available in the supplementary information.

vertebrates (Botterell et al., 2019; Everaert et al., 2022; Foley et al., 2018; Welden and Cowie, 2016). The few studies that have explored how MPs impact the energy allocation of organisms indicate elevated maintenance costs in oysters exposed to 2 and 6  $\mu\text{m}$  polystyrene beads (Sussarellu et al., 2016) and a negative impact of 2  $\mu\text{m}$  polystyrene beads on the energy metabolism of mussels at cellular level, which is not restored in a short-time period (Shang et al., 2021). Negative effects can potentially not be observed in the case of exposures of healthy organisms. For example, sea anemones previously bleached were unable to select for microplastic ingestion when compared to healthy specimens, illustrating that organisms under previous stress can be more vulnerable to MPs (Romanó de Orte et al., 2019). There are however indications that ingestion of polystyrene MPs in low doses has no effect on feeding rates and growth to the amphipod *Echinogammarus marinus* (Bruck and Ford, 2018) and that PET microplastics do not affect survival, development, metabolism and feeding activity of the freshwater copepod *Gammarus pulex* (Weber et al., 2018). Mixtures of particles of multiple size ranges have been used to expose microalgae at environmental relevant concentrations, with no reported growth rate reductions (Niu et al., 2021). The detrimental impacts of MPs ingestion can be further reversed in the particular case of biofouled particles, where biofilms are a source of nutrients to microinvertebrates, contradicting assumed starvation effects (Amariei et al., 2022), but the role of MPs-associated biofilms is still poorly known. Contrasting reported effects of MNPs can be linked to differences in size, volume, area, aspect ratio, shape of MPs (Koelmans et al., 2022b), highlighting the need for more realistic assessments, which should move beyond a single-particle single-stressor framework to a broader assessment and that accounts for the vulnerability of biological systems.

When vital processes (growth, reproduction, etc) of biota at lower trophic levels are negatively impacted by MPs, their populations may decline, with repercussions at higher trophic levels (Botterell et al., 2019; Foley et al., 2018). Environmentally relevant ecotoxicity work with invertebrates exposed to MPs should clarify sublethal endpoints, as effects of MP are likely to occur more subtly at lower levels of biological organisation, which can impact throughout other levels of biological organisation and food webs. Although MPs-induced effects in ecosystems have not yet been established, the few published studies at population and community levels suggest that ingestion of plastics particles have the potential to reduce the physiological condition of individuals, thereby lowering their chances of survival or reproduction and, in turn, lowering the population growth rate or changing the community composition (Everaert et al., 2022; Green, 2016; Green et al., 2017; Redondo-Hasselerharm et al., 2018; Ziajahromi et al., 2018). In freshwater communities, the exposure of a dwelling insect larvae to MPs in

sediments (500 particles / kg) can lead to less emerging adults, and of lower body mass, due to low egestion levels and clogging of the individuals' gut (Ziajahromi et al., 2018). Also in freshwater communities, exposure of high doses of PS microplastics in sediment (40% sediment dw) did not induce effects in five out of six tested invertebrate species, indicating a low risk of microplastics (Redondo-Hasselerharm et al., 2018). However, in the same study, the authors demonstrated that in the only specimens (copepod) affected there was a size selective uptake of MPs, coupled to slow egestion rates (Redondo-Hasselerharm et al., 2018), indicating that energy allocation to key processes may have been impacted. In another study, meiobenthos seawater communities differed in sediments exposed to microplastics (25 - 80  $\mu\text{g} / \text{L}$ ) when compared to control levels (Green, 2016; Green et al., 2017), with reported decrease in species richness and loss of biomass of invertebrate species (Green, 2016). Recently, and based on a mechanistic model to assess the individual sublethal effects due to MPs impact at population level, Everaert et al., 2022 observed that at  $593 \pm 376$  MPs / L the population equilibrium density of a marine copepod would decrease by 50%, a figure that is a fourfold lower than the effect concentration at individual level, indicating a higher sensitivity of populations. The studies above mentioned, which all focus on single MPs-stressors, have provided crucial building blocks to understand the main mechanisms of action of MPs potential toxicity over biota, but there is now a need to explore more realistic scenarios.

A contextualised vision of the magnitude of the impact of complex mixtures of MPs in real-world scenarios is urgently needed. To better understand and quantify MPs effects and risk in ecosystems (at community and population levels) the next crucial step is to assess the type of particles, sizes, and proportions in a MP mixture accessible for ingestion to each organism. Reports of adverse effects of MPs on aquatic species are mostly assessed using pristine particles, often of regular shape, of one single type of polymer and at exposures higher than those found in the environment (Botterell et al., 2019; Bucci et al., 2020; Lenz et al., 2016). Meta-analyses of existing data (Everaert et al., 2018; Koelmans et al., 2020) have provided good indications of general patterns of MPs effects, concerning exposures to single type of particles, as well as provisional safe thresholds for MPs risk, but are often hampered due to limited quality of the few data available (De Ruijter et al., 2020). Assessing MPs risk, i.e., the probability or likelihood of adverse consequences (hazards) occurring to an exposed ecological entity (Newman, 2010; SAPEA, 2019), is an evidence-based process that requires reliable data to assist regulators and policymakers in prioritising mitigation actions (Catarino et al., 2021). To address the lack of relevant data for MPs risk assessments (De Ruijter et al., 2020), current research should focus on investigating the effects of representative MPs mixtures, reproducing realistic envi-

ronmental settings, in terms of polymer composition, size, shape and concentration, and within the context of a changing environment.

### Multiple stressors: microplastics and global change

In real case scenarios, environmental MPs and global change driven stressors do not operate in isolation. Stressors' impacts can combine additively (where the net effects of multiple stressors are equal to the sum of their single effects) or interact in a synergistic or antagonistic manner (where the sum of the net effects is greater or less, respectively, than the sum of separate effects, but in the same direction as the individual responses) (Cooley et al., 2022; Johnson and Penaluna, 2019). The combination of stressors can further be a reversal interaction (where the net response is in the opposite direction from the expected response) (Johnson and Penaluna, 2019), lead to a chain interaction (when a stressor alters the prevalence of another one), or finally to a modification interaction (when a stressor alters the prevalence and per capita effect of another one) (Geary et al., 2019). The major challenge relies then in the assessment of responses of organisms, populations and ecosystems to MPs in a context of global change, which is still a very recent field of interest. The induced effects of single global change stressors (OW, MHW, OA, OD) in organisms, populations, communities and ecosystems, are well documented, and The Intergovernmental Panel on Climate Change (IPCC<sup>1</sup>) has compiled high confidence model-based future predictions of their effects (Cooley et al., 2022). Research concerning the effects of MNPs is still limited in its scope, and the first attempts to establish a safety threshold have only recently been established (Everaert et al., 2020).

Despite the very limited number of studies available up to now (Fig. 1, Supplementary Table S2), there are indications that MNPs have the potential to interact with OW and OA, and impact ingestion and digestive processes, energy allocation, growth, and fecundity of aquatic organisms. The interaction of MPs with OA can induce in mussels a decrease in the expression of oxidative stress biomarkers, in *Mytilus galloprovincialis* (Provenza et al., 2020) and *Mytilus coruscus* (Wang et al., 2020); and lead to inhibition of digestive enzymes (Wang et al., 2020). In embryonic and larval stages of the sea urchin *Paracentrotus lividus*, MPs exposure combined with acidification (Piccardo et al., 2020) and combined with OA and OW (Bertucci and Bellas, 2021), lead to smaller larvae and a higher number of development abnormalities. However, Piccardo et al. 2020 state that the interaction of MPs and OA did not induce consistent combined responses, and that sea urchin larvae were significantly sensitive to food availability. In the freshwater crustacean *Daphnia* sp., treatments with increased temperature induced an accelerated ingestion of MPs which induced ultrastructural abnormalities in intestinal epithelial cells (Lyu et al., 2021), altered energy allocation (Lyu et al., 2021) and induced changes in growth and fecundity (Chang et al., 2022). Similarly, in freshwater gammarid amphipods, the metabolic rates of organisms have decreased when organisms were exposed to MPs and higher temperatures, but in this case, there was no indication of altered feeding rates (Kratina et al., 2019). However, Reichert et al., 2021 observed that in some species of reef building corals, MPs exposure led to an aggravated response to thermal stress, whereas in others there was a mitigating effect, indicating that sensitivity to multiple stressors varies greatly across even closely related organisms.

Up to now, there has been no studies on combined MPs and global change stressors at population, community or ecosystem level. Current indications suggest, for instance, that particularly vulnerable species or

organisms (Romanó de Orte et al., 2019) may be at higher risk of combined effects of MPs and other stressors, and these may impact higher levels of biological organisation. Other interactions of MPs and global change have led to questions on whether the increased rain regimes and sediment resuspension events led by climate change will impact the load of MPs in water bodies that reach coastal environments (Zhang et al., 2020). Furthermore, the increased grazing on MPs by zooplankton could also further accelerate oxygen loss in marine ecosystems due to an additional remineralisation pressure (Kvale et al., 2021). Another example is the question on whether MPs would impact on the capacity for oceans to assimilate CO<sub>2</sub> as MPs are likely to impact phytoplankton and zooplankton growth and development and to indirectly affect the biological pump and carbon stocks (Shen et al., 2020). To further assess their interactions in the environment, quantitative assessment of effects and environmental data acquisition are critical to follow the evolution of potential impacts feedback-loops.

### The particular case of nanoplastics

The occurrence of MPs and the predicted co-occurrence of NPs in the environment indicates that organisms can be exposed to a continuum of complex mixtures of MNPs, with further interaction with multiple stressors. The environmental observation of NPs still remains challenging (Paul-Pont et al., 2018), but in laboratory settings the fragmentation of MPs to NPs has been established via weathering phenomena (Mattsson et al., 2021), and via interactions with biota such as digestive fragmentation from krill (Dawson et al., 2018) or microorganism-induced fragmentation (Karkanorachaki et al., 2022). This fragmentation is expected to occur in the environment (Paul-Pont et al., 2018), and the number of NPs is predicted to be higher than that of MPs (Lenz et al., 2016). It is also known that NPs agglomerate and interact with larger particles and microorganisms (Summers et al., 2018), which may influence their environmental fate and their probability of being ingested. The ingestion of NPs can lead to egestion as in the case of MPs (Al-Sid-Cheikh et al., 2018; Dawson et al., 2018), but a small fraction could potentially cross epithelial barriers in the gut, i.e. translocate (Al-Sid-Cheikh et al., 2018; Clark et al., 2022). Exposure of organisms to NPs raises therefore further concerns beyond gut blockage or starvation induction (Paul-Pont et al., 2018), but once more the large majority of current NP effect assessments lacks environmental relevance, even if elucidating for modes of action (Asselman, 2022). The first steps to estimate risk assessment of NPs have taken place, with the derivation of species sensitivity distributions (SSDs), essential in estimating a hazardous concentration for 5% of the species (HC5) (Takeshita et al., 2022). However, to the best of the authors knowledge, no studies have considered exposure of organisms to heterogeneous and complex mixtures of MNPs, and the large majority of NPs exposures are limited to the use of pristine polystyrene (PS) or polyethylene (PE) spheres (Paul-Pont et al., 2018). In what concerns the effects of NPs together with global change-related stressors, current knowledge is limited to one study, which indicates that exposure to NPs and low pH can lead to a delay in the embryonic and larval development of Antarctic krill (Rowlands et al., 2021). The effect assessment of NPs therefore requires studies to move towards more realistic scenarios, in the context of global change, to provide information required for relevant ecological risk assessments.

### Environmental data acquisition

Data acquisition of environmental data is critical to perform effect assessments that are representative of realistic scenarios, and which lead to meaningful effects assessments. Data acquisition concerning global change drivers has been performed extensively, e.g. by NOAA (National Oceanic and Atmospheric Administration NOAA, 2021), ARGOS (ARGOS 2022 - Integrated global Earth observations) or Copernicus (Copernicus, 2022 - the European Union's Earth Observation Programme), but the quantification of MPs in environmental matrices (e.g.,

<sup>1</sup> The IPCC ([www.ipcc.ch](http://www.ipcc.ch)) is the United Nations (UN) body for assessing the science related to climate change, and which gathers evidence-based information thanks to an international panel of experts that regularly assesses and predicts effects of climate change stressors from an ecological and a human point of view.

sediment, water, and biota) has only recently started, with a very limited number of reports for NPs. The major challenges in acquiring accurate and comparable data on MNPs are related to quality assurance and quality control (QA/QC) issues (Brander et al., 2020; Koelmans et al., 2019), to the use of multiple and not yet harmonised identification methodologies, and to the complexity of extracting and distinguishing MNPs from other environmental particles (Cowger, 2020). Nanoplastics detection in environmental samples have an additional degree of complexity due to the current detection limits of observation instrumentation based on microscopy (e.g. fluorescence microscopy), spectroscopy (FT-IR and Raman) (Brander et al., 2020). There are recent insights into the detection of environmental NPs (Materić et al., 2020) using thermal desorption–proton transfer reaction-mass spectrometry, but the implementation of systematic observations will still require major efforts. Even though research on MNPs is evolving rapidly, only now are the first microplastic surveying activities being included in monitoring programmes, at a European Union level e.g. Marine Strategy Framework Directive (European Commission, 2021), or at regional seas level, e.g., OSPAR Commission (OSPAR, 2022). There are currently no official environmental targets or assessment criteria for MNPs in the marine environment (OSPAR Commission, 2020), but once in place these will greatly contribute to the knowledge gaps on MNPs fate and distribution in the marine environment, key for improved exposure effects and risk assessments.

### Modelling effects for informed management decisions

To answer pertinent questions on the effects of the interaction between MNPs and global change, high-quality datasets should be integrated in the development of models that assist in defining projections of potential future effect scenarios in the marine environment. Besides the use of data-driven approaches, Pirota et al., 2022 suggested the use of increased stringent mechanistic assumptions, which increase the predictive power beyond the observed range of doses, even if with a risk that the assumptions may not be correct (e.g. when factorial designs are used). Most mechanistic models are fit for purpose and enable the understanding of causal relations between the functioning of ecosystems and the potential impact of human induced stressors. Mechanistic assumptions can be based on known dose-response and forcing functions (e.g. thermal performance curves or behavioural dose-response functions) (Chagaris et al., 2020; Everaert et al., 2022) and models can have a high predictive power, with a wide management applicability (Pirota et al., 2022). The introduction of forcing functions can be implemented for a large suite of potential stressors, and thus inherently allow to assess the combined effects of stressors. Mechanistic models are thus be calibrated based on experimental or field data, from which what-if simulations can be performed to understand the effects of environmental conditions shifts for the level of biological organization assessed (Everaert et al., 2015). Examples of models that connect different biological levels of organisation based on mechanistic information are the adverse outcome pathways (AOPs) in ecotoxicology, the dynamic energy budget models (DEB) when stressors interfere with the baseline flow of energy acquisition and allocation, and the individual-based models (IBM) where “individual agents, characterised by internal state variables, are simulated to interact with dynamic landscapes over time” (Pirota et al., 2022). The use of AOPs has been suggested as an innovative strategy in Environmental Risk Assessment (ERA), linking molecular and cellular shifts to higher level organismal effects (Ankley et al., 2010; Villeneuve et al., 2014). The AOP framework may be of particular interest in the case of exposure of organisms via both inhalation and ingestion pathways, in particular in the case of NPs which have the ability to translocate. The use of the DEB theory is applicable to assessing the effects of MPs at an individual level, for example when ingestion is assumed as a exposure pathway (Everaert et al., 2022). Microplastics therefore can reduce the energy reserve and further altered the energy balance between growth, maintenance, maturation and re-

production (Everaert et al., 2022; Sussarellu et al., 2016). When coupling DEB with IBM models, the individual-level effects from standardised toxicity data enable extrapolation of effects to population level (Vlaeminck et al., 2021). In addition, studies have parametrized DEB models with dependency on environmental conditions such as temperature and pH (Jager et al., 2016; Koch and De Schampelaere, 2019), and have demonstrated the applicability of DEB-IBM models in multiple stressors effect assessments (Maynou et al., 2020). Another approach suitable to unveil and integrate the potential combined effects of multiple stressors on marine ecosystems and their functioning is the use of probabilistic techniques, which have been used for MP risk assessment (Adam et al., 2021; Everaert et al., 2020), and which could potentially be expanded to include MNPs complex mixtures and other environmental stressors.

Ecological models can further establish predictions on effects that are impractical to assess via experimental work due to technical and logistical constraints or as set-ups at population and community levels are often time and cost demanding. Mechanistic food web modelling, for example, is an approach that can establish mass balance models of marine ecosystems (Christensen and Walters, 2004; Colleter et al., 2015). These models use functional groups (e.g. top predators, fish, invertebrates, etc) as units that have “biomass” as a common denominator (Pint et al., 2021) and which are connected by trophic interactions. By using this ecological network approach, it is possible, for instance, to identify and quantify major energy and biomass flows in an ecosystem and explore management policies options (Freitag et al., 2019). Ecological models are particularly important for environmental decision support as they enable the understanding of how policies and management scenarios can improve ecosystems functioning and services (Schmolke et al., 2010). Models can be further useful as tools to assist key stakeholders (managers and policymakers) to take evidence-based decisions thanks to probabilistic predictions, for example using Bayesian Belief Networks (BBNs) (Leone et al., 2022).

### Conclusion and perspectives

The ubiquitous distribution and persistence of plastic litter, including MNPs, in the environment are of concern for both the public and policymakers. Recently, the United Nations (UN) Environment Assembly has agreed to launch negotiations on a legally binding international agreement to act against plastic pollution, from production to disposal (2 March 2022, Nairobi, Kenya) (UNEP, 2022). The UN plastic pollution resolution complements existing initiatives and agreements that stress the importance of contextualising plastic pollution within the need for a circular and sustainable ocean economic development (The Ocean Panel, 2022), such as the European Commission (EC) Green Deal and the Circular Economy Plan (European Commission, 2022). The marine environment is under extreme pressure from human activities (Cooley et al., 2022), and the mitigation of stressors such as global change drivers and MNPs requires a holistic framework that aligns environmental data acquisition, quantitative assessment of effects and risk, and models and predictions of future impacts. No topic, global change versus plastic pollution, is of higher importance (Horton, 2022), and the assessment of realistic effects of MNPs on all biological levels of organisation must consider the co-occurrence in the environment of stressors such as ocean warming (OA), ocean acidification (OA), ocean deoxygenation (OD), extreme heat waves (EHW), amongst others. Current, but still limited, evidence indicates that MNPs interact with global change stressors and can impact on aquatic organisms’ processes such as ingestion and digestion, energy allocation, growth, and fecundity. The potential impact of this interaction at population levels is largely unknown, as well as the effects of heterogenous and complex mixtures of particles, representative of environmental MNPs. Experimental work using single stressors (e.g., single particle type, isolated effect assessments of MPs or NPs, etc.) can be used to inform on experimental design and interpretation of elaborated multiple stressors studies. The acquisition of relevant and

high-quality data will enable the elaboration of models that can predict effects at different biological organization levels (e.g., AOP for molecular to individual levels, or DEB-IBM for individual to population levels), or inform on risk assessment (e.g., using probabilistic approaches). Relevant effect data of stressors of interest can be further used in ecological models by integrating the corresponding forcing functions, useful to run what-if scenarios, which are key to inform stakeholders on how the implementation of mitigation measures can result in shifts in ecosystem services, for instance. Broadening the scope of MNPs effect assessments requires immediate attention from the research community, to provide information to stakeholders on the vulnerability of marine species and ecosystems, under current and future environmental conditions.

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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.

## CRediT authorship contribution statement

**Ana I. Catarino:** Conceptualization, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Jana Asselman:** Conceptualization, Investigation, Writing – original draft, Writing – review & editing. **Zhiyue Niu:** Conceptualization, Investigation, Writing – original draft, Writing – review & editing. **Gert Everaert:** Conceptualization, Supervision, Writing – original draft, Writing – review & editing.

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## Supplementary materials

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