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Towards a unified study of multiple stressors

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1 **Title:** Towards a Unified Study of Multiple Stressors: Divisions and Common Goals Across
2 Research Disciplines

3

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40

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42 Antagonism, Combined Effects

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51 **Abstract:**

52 Anthropogenic environmental changes, or ‘stressors’, increasingly threaten biodiversity and
53 ecosystem functioning worldwide. Multiple-stressor research is a rapidly expanding field of
54 science that seeks to understand and ultimately predict the interactions between stressors.
55 Reviews and meta-analyses of the primary scientific literature have largely been specific to
56 either freshwater, marine or terrestrial ecology, or ecotoxicology. In this cross-disciplinary
57 study, we review the state of knowledge within and among these disciplines to highlight
58 commonality and division in multiple-stressor research. Our review goes beyond a description
59 of previous research by using quantitative bibliometric analysis to identify the division
60 between disciplines and link previously disconnected research communities. Towards a
61 unified research framework, we discuss the shared goal of increased realism through both
62 ecological and temporal complexity, with the overarching aim of improving predictive power.
63 In a rapidly changing world, advancing our understanding of the cumulative ecological
64 impacts of multiple stressors is critical for biodiversity conservation and ecosystem
65 management. Identifying and overcoming the barriers to interdisciplinary knowledge
66 exchange is necessary in rising to this challenge. Division between ecosystem types and
67 disciplines is largely a human creation. Species and stressors cross these borders and so
68 should the scientists who study them.

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76 **1. Introduction**

77 The most severe threats to global biodiversity and ecosystem functioning are anthropogenic
78 environmental changes, or “stressors,” such as habitat loss, climate change, pollution and
79 invasive species (1, 2). These stressors often interact in complex and unexpected ways (3-6).
80 Multiple-stressor research seeks to understand and predict interactions between stressors.
81 Importantly, due to these interactions the combined effect of two or more stressors is
82 frequently more than (synergistic) or less than (antagonistic) expected based on their
83 individual effects (7, 8). The study of multiple stressors is not a novel pursuit in science;
84 toxicologists, and later ecotoxicologists, have been identifying the combined impact of
85 multiple chemical stressors on individual organisms or populations for almost a century (9,
86 10). Multiple-stressor research has now expanded to more diverse stressor combinations and
87 has become a prominent feature of global change biology. Consequently, the concepts and
88 terms used in the multiple-stressor literature have become common in mainstream biology.
89
90 Aquatic, terrestrial, and ecotoxicological investigations into multiple stressors differ greatly in
91 their approach. In the freshwater and marine ecology literature, numerous studies have
92 measured biological responses to specific stressor combinations (3, 5). Such work has been
93 conducted across the globe, from the Arctic (11) to the Antarctic (12), and has focused on
94 virtually all taxonomic groups, including bacteria (13), algae (14), invertebrates (15),
95 amphibians (16), and fish (17). Parallel to this research, and with almost no lateral exchange,
96 the effects of multiple stressors on ecosystems have been the focus of many terrestrial
97 experiments (18-20). Contrary to the freshwater and marine literature, the response variables
98 of interest in terrestrial studies are mostly the fluxes and pools of matter such as water,
99 carbon, nitrogen or other nutrients. Another discipline that has dealt with impacts of multiple
100 stressors is ecotoxicology, which focuses on the effects of chemical pollutants and their

101 interactions with other stressors (6, 21, 22). Although freshwater, marine and terrestrial
102 subdisciplines exist within ecotoxicology, they share a basic scientific foundation (e.g.
103 methods, journals and conferences), which merits their aggregation as one discipline in this
104 review.

105

106 Regardless of differing approaches, the underpinning concepts of multiple-stressor research
107 are similar across the different disciplines. Despite this, exchange and cross-fertilization of
108 ideas and conceptual models has been limited. For example, the co-tolerance concept (23), a
109 number of stressor interaction classification systems (e.g., 7), and various null models
110 predicting the combined effect of stressors (e.g., 24, 25) have virtually escaped the terrestrial
111 ecology community (4, 18, 26). Moreover, models and methods developed in the context of
112 ecotoxicology have largely been ignored in aquatic and terrestrial ecology (27). Even reviews
113 and meta-analyses of the multiple-stressor literature have primarily been specific to either
114 freshwater (5), marine (3) or terrestrial systems (18), or to ecotoxicology (6) (but see: 28, 29).

115

116 Differences in terminology attest to the disconnection of freshwater, marine and terrestrial
117 ecologists, as well as ecotoxicologists, from each other. For example, while the terms
118 “stressors”, “antagonism” and “synergism” are common within the freshwater, marine and
119 ecotoxicology literature (5, 24, 30), many terrestrial and some marine ecologists often use the
120 terms “drivers/factors”, “dampening” and “amplification”, respectively (18, 26, 31, 32). Other
121 terms such as “cumulative effects”, “combined effects”, “net effects” or “interactive effects”
122 are used across all disciplines, but without consistent definitions (3, 33, 34). The pre-existing
123 separation among scientific disciplines further contributes to this division in multiple-stressor
124 research, exemplified by how ecologists tend not to cite work carried out in systems different
125 from their own (35, 36).

126

127 A better exchange between the different disciplines studying multiple stressors would be
128 highly desirable. The separation of disciplines, including inconsistency in the terminology,
129 hampers progress in multiple-stressor research because scarce resources are wasted due to the
130 parallel development of similar methods and tools in different disciplines. Equally,
131 incomplete literature searches and meta-analyses create an ignorance of the complete
132 evidence, which can mislead research directions, impede the spread of ideas and slow down
133 development of overarching theoretical concepts. In this cross-disciplinary review we use
134 quantitative bibliometric analysis to identify and illustrate the division between multiple-
135 stressor researchers from different disciplines, we discuss qualitative differences in methods and
136 terminology between the disciplines, and we provide a common glossary to harmonise concepts
137 and terminology. Subsequently, we identify and discuss three common research goals that all
138 multiple-stressor researchers share towards a unified research framework, specifically: (i)
139 increased ecological complexity, (ii) increased temporal scale and realism, with the overarching
140 aim of (iii) improving predictive power.

141

142

143 **2. Bibliometric Analysis**

144 **2.1 Methods**

145 Using terms identified during our cross-discipline review we performed a search of the *ISI*
146 *Web of Knowledge* database (<https://apps.webofknowledge.com>) to collect publications from
147 the multiple-stressor literature (SM1). Next, we constructed citation networks where nodes
148 represent specific publications and links indicate a citation between connected publications.
149 Clustering algorithms and citation analysis were used to group publications that cite each
150 other more than they cite other publications in the same network (37). To enhance visibility,

151 only the most influential publications (top 300 most cited) were used to construct the citation
152 networks. Given that this was biased towards marine and freshwater publications, the 25 next
153 most highly cited terrestrial and ecotoxicological publications were added to ensure a similar
154 number of publications across disciplines. The largest connected network (150 publications:
155 SM2) from this pool of 350 publications was selected, ignoring publications outside the
156 multiple-stressor literature. We also created term networks, based on the 150 multiple-stressor
157 publications, using text-mining techniques to identify different clusters of terminology. The
158 publications and terms were manually assigned to one of the disciplines. For details on the
159 bibliometric analysis, see SM2.

160

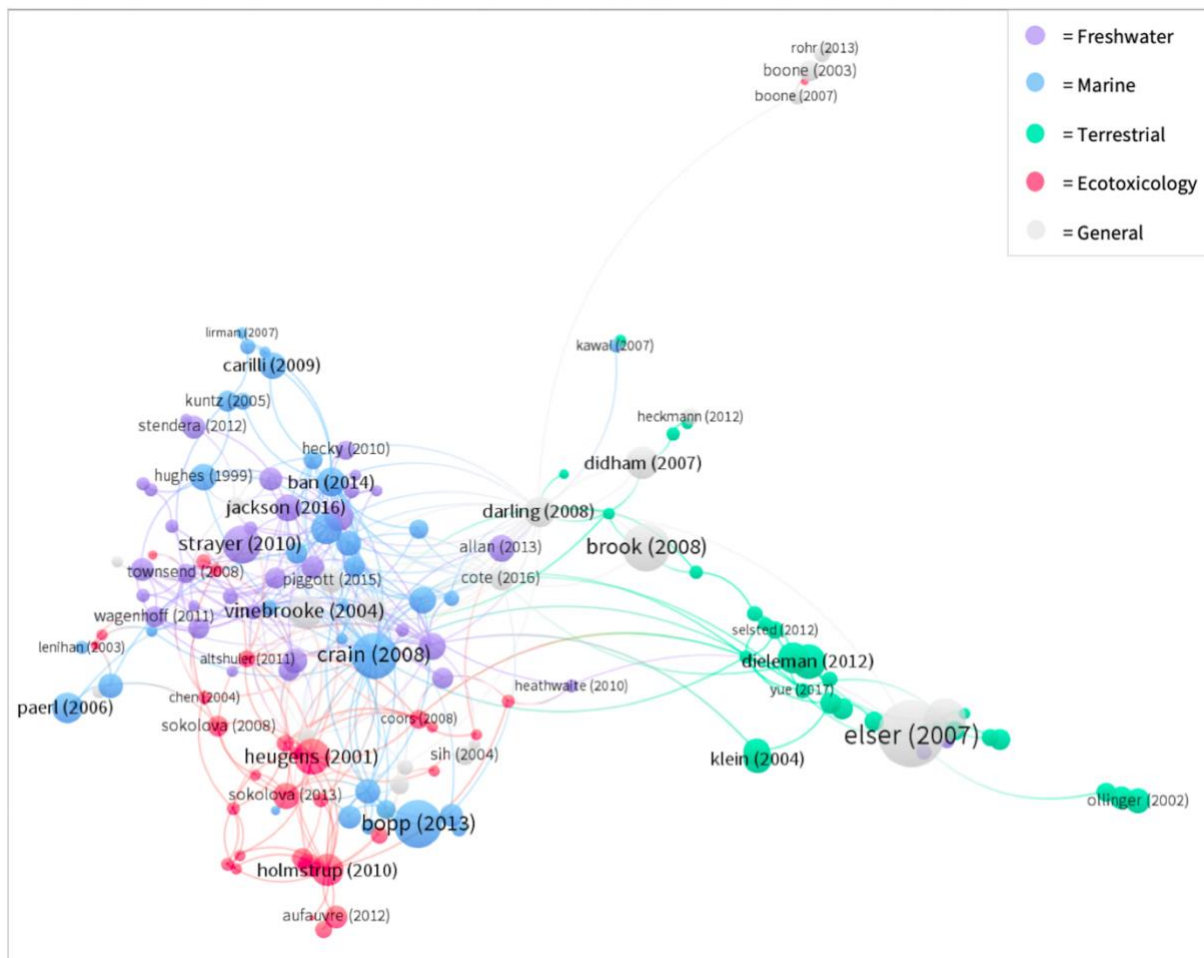
161 **2.2 Results**

162 A citation network of 150 publications from the multiple-stressor literature with colours
163 representing clusters emerged from our analysis (SM3). The size of the nodes was based on
164 the number of citations normalized by age of publication. When the size of the nodes was
165 based on the number of links in the network, emphasis was put on different nodes (SM4).
166 Supplementing our networks with additional publications reduced a bias in terms of nodes but
167 may not have reduced a bias in terms of links (citations); on average the freshwater and marine
168 publications had more citations than publications from the other disciplines. Consequently, we
169 constructed larger networks using a lower common threshold of citations resulting in networks
170 based on the 500, 1000, 1500 and 2000 most highly cited publications (SM5). Although these
171 larger networks are much more difficult to read, clustering patterns similar to SM3 are
172 conserved.

173

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176

177 **Figure 1:** Citation network where the nodes represent publications and the links indicate the
 178 presence of a citation between connected publications. The size of the nodes represents the
 179 number of citations normalized by age. The distance between nodes is calculated using a
 180 citation analysis algorithm which determines the relatedness of items based on the number of
 181 times they cite each other. The colours of the nodes and their links represent the disciplines
 182 they belong to.

183

184 Customizing the colours of the nodes and links to represent the different disciplines reveals
 185 the division between disciplines (Figure 1). Some of the key papers in the multiple-stressor
 186 literature are cited across disciplines and are found towards the center of the networks (7, 8,
 187 23, 28, 29). Although the freshwater, marine and ecotoxicology literature clearly have their
 188 own clusters, these disciplines substantially overlap (particularly freshwater and marine). In

189 contrast, the terrestrial publications form a distinct cluster that is only connected to the rest of
190 the network via five key nodes, which are mostly meta-analyses or reviews (18, 28, 29, 34,
191 38).

192

193 A heat map was produced to quantify the division between disciplines in the citation networks
194 (SM6). The terrestrial publications are found almost exclusively in cluster 1 (82.8%) of the
195 citation network (SM3). The ecotoxicological publications are found primarily in cluster 4
196 (54.8%). The freshwater publications are found primarily in clusters 2 (44.1%) and 6 (23.5%).
197 The marine publications are well represented in all clusters in the network except for clusters
198 1 and 4.

199

200 In the term network, nodes towards the center of the network (e.g. effect, interaction,
201 response) are used by all multiple-stressor researchers, whereas some nodes at the edges of
202 the network are discipline-specific (Figure 2). The coloured nodes have been assigned to
203 specific disciplines to outline the approximate location of disciplines in the network (full list
204 of terms in SM7). These coloured terms act as markers against which the location of general
205 terms of interest can be compared. For example, the term “multiple stressor” is found towards
206 the edge of the network near freshwater, marine and ecotoxicological terms; it is on the
207 opposite side of the network from where the terrestrial terms are. Similarly, the term “global
208 change driver” is found among the terrestrial terms and away from the terms specific to the
209 other disciplines.

210

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212

213

224 **3. Synthesis**

225 As well as bibliometric analysis, a review of the literature was carried out to investigate how
226 disciplines differ in their study of multiple stressors (summarized in SM8). Our aim was to
227 compare the predictor and response variables, methods and key findings from meta-analyses
228 of multiple-stressor research across disciplines. One of the key findings from our review was
229 that multiple-stressor researchers from different disciplines, despite studying fundamentally
230 the same phenomena, are using different terminology for predictor variables and interactions.
231 Equally, the most common predictor and response variables studied differ among disciplines
232 (Table 1), which likely reflects alternative perspectives on which stressors are most important
233 (36).

234

235 Another difference between and within disciplines is how researchers define a stressor. Many
236 researchers associate stress with a negative biological response (23, 39) but others argue that
237 the effect of any stressor is context dependent and can be positive or negative (7, 29, 40). For
238 example, all common stressors (predictor variables) listed in Table 1 can cause positive or
239 negative effects depending on the study species or the response variable. Another element to
240 consider is whether a stressor can be natural, or only anthropogenic. Some researchers keep
241 the definition as broad as possible (29, 41) whereas others state that what separates a stressor
242 from a “driver”, “factor” or “disturbance” is that it is anthropogenic (7, 42). For the latter
243 definition, it is important to note that natural factors such as predation or herbivory can
244 become stressors under human modification.

245

246

247

248 **Table 1:** Comparison of multiple-stressor research across freshwater, marine and terrestrial
 249 ecology and ecotoxicology.

Discipline	Terminology for predictor variables	Terminology for interactions	Common predictor variables	Common response variables	Key references
Freshwater	Stressor	Additive Synergistic Antagonistic Reversal	Increased temperature Altered flow Nutrients Toxicants Habitat modification Invasive species	Population metrics Functional traits Biodiversity	(5, 43, 44)
Marine	Stressor Driver	Additive Synergistic Antagonistic	Increased temperature Acidification Pollutants Nutrients High/low salinity Hypoxia Habitat modification	Physiology Population metrics Functional traits Biodiversity	(3, 30, 45)
Terrestrial	Factor Driver	Additive Synergistic Antagonistic Dampening Amplifying Counteracting	Increased temperature Increased CO ₂ Land use change Nutrient modification Altered precipitation Invasive species	Fluxes and pools of elements, compounds and nutrients Productivity Biodiversity	(18, 34, 46)
Ecotoxicology	Stressor Toxicant Toxic chemical	Additive Synergistic Antagonistic	Toxicants Increased temperature Salinization Drought Pathogens or predators	Physiology Population metrics Biodiversity	(6, 22, 24)

250

251

252 There is a clear division between terrestrial researchers, who tend not to use the term

253 “stressor”, and the rest of the multiple-stressor community. Terrestrial ecology has provided

254 crucial evidence of the combined effect of stressors, but the language used leads to multiple-

255 stressor meta-analyses missing these studies. That is because rather than using the common

256 terminology of multiple-stressor research (e.g., stressor, antagonism or synergism), some
257 studies only refer to the specific factors examined and describe effects as “dampening”,
258 “amplifying” or “counteracting forces” (26, 46, 47). For example, in Darling and Côté’s (28)
259 meta-analysis of factorial experiments examining the effects of multiple stressors on animal
260 mortality in freshwater, marine and terrestrial communities the keywords used in their search
261 included “synergy”, “antagonism” and “stress” but lacked “amplifying”, “dampening” or
262 “factor/driver”. Potentially as a result of this, only four of the 112 experiments in the meta-
263 analysis were conducted with terrestrial organisms (excluding amphibians) (28). Hence, meta-
264 analyses are useful in that they can identify knowledge gaps and pose new questions, but they
265 reinforce division between disciplines when restricted to certain search terms. Another
266 potential issue is that the same word can have different meanings or connotations in different
267 disciplines, although this is difficult to quantify. For example, the word “stressor” is often
268 associated with negative effects, whereas some researchers, particularly from aquatic
269 disciplines, employ a more neutral interpretation (7, 29, 40). This highlights the potential
270 importance of metaphors in creating barriers between disciplines.

271

272 As a result of the division between these research communities, certain ideas or approaches
273 can become confined to different disciplines. For example, the terminology and concept of
274 global versus local stressors is often mentioned in the marine literature (14, 48, 49) but is
275 rarely discussed elsewhere. Similarly, it seems that only freshwater ecologists use the term
276 “reversals” when one stressor reverses the effect of another (5). For instance, Christensen *et*
277 *al.* (38) found that a positive effect of acidification on phytoplankton became negative when
278 warming was introduced. Ecotoxicologists have developed considerable theory on null model
279 selection (24, 50), which is only now being introduced to other communities of multiple-
280 stressor research (27). Novel concepts and approaches do not need to be (re-)discovered

281 multiple times and all disciplines would benefit from a mutual exchange of ideas. We provide
 282 a glossary of terms (Table 2), with synonyms grouped, as a step towards the unification of
 283 multiple-stressor research.

284

285 *Table 2: Glossary of widely used terms and concepts in multiple-stressor research. When*
 286 *multiple terms are grouped together we consider them synonyms.*

Terms/Concepts	Our Definition	Source
Stressor Factor Driver	Any natural or anthropogenic variable that causes a quantifiable change, irrespective of its direction (increase or decrease), in a biological response. However, many researchers associate the term “stressor” with an anthropogenic variable that has a negative impact.	(29)
Multiple Stressors	Two or more co-occurring or sequential stressors.	n/a
Combined effect Cumulative effect Net effect	The aggregate effect of multiple stressors and their interactions.	n/a
Stressor Interaction	Modification of a stressor’s intensity or the sensitivity of an organism or ecosystem towards this stressor by another stressor or multiple other stressors. Thus, the term refers to the interaction between stressors in the real world. By contrast, concepts such as the multiplicative null model rely on mathematical interactions that do not necessarily imply interactions in the real world. Not to be confused with biotic interactions among organisms.	(27)
Additive	When the combined effect of multiple stressors is equal to the sum of their individual effects, i.e. no interaction effect.	(8)
Antagonistic Dampening Counteracting	Interactions between stressors that result in a lesser combined effect than that predicted by a null model (i.e. an interaction between stressors making their observed net effect less than expected).	(27)
Synergistic Amplifying	Interactions between stressors that result in a greater combined effect than that predicted by a null model (i.e. an interaction between stressors making their observed net effect more than expected).	(27)
Reversal	Interactions that result in the combined effect of two stressors being opposite in direction (negative or positive) from that of the sum of their single effects.	(5)
Null Models	A model that predicts the combined effect of multiple stressors assuming the absence of interactions among stressors as defined above. However, some null models contain mathematical interactions to capture stochastic aspects in the action of two stressors, for example the multiplicative null model.	(27)

Ecological Surprises	Scenarios where the mechanisms of stressor interactions are not understood and predictions based on null models fail.	(51)
Discipline	A field of science that is represented by specific journals and conferences and consequently establishes a community of scientists. Disciplines are typically taught and researched separately as part of higher education.	n/a

287

288

289 **4. Towards a Unified Research Framework**

290 Despite the division between disciplines described above, all multiple-stressor researchers
 291 share the same goals. Elements of these common goals have been identified before but are
 292 scattered across the literature in both primary research and reviews. Here we integrate and
 293 develop on these shared research goals of increased (i) ecological complexity, (ii) temporal
 294 scale and realism, and (iii) prediction. Our conceptual framework offers a future direction for
 295 multiple-stressor research (Figure 3). Greater interdisciplinary knowledge-exchange,
 296 facilitated by this review, is a key component of this framework.

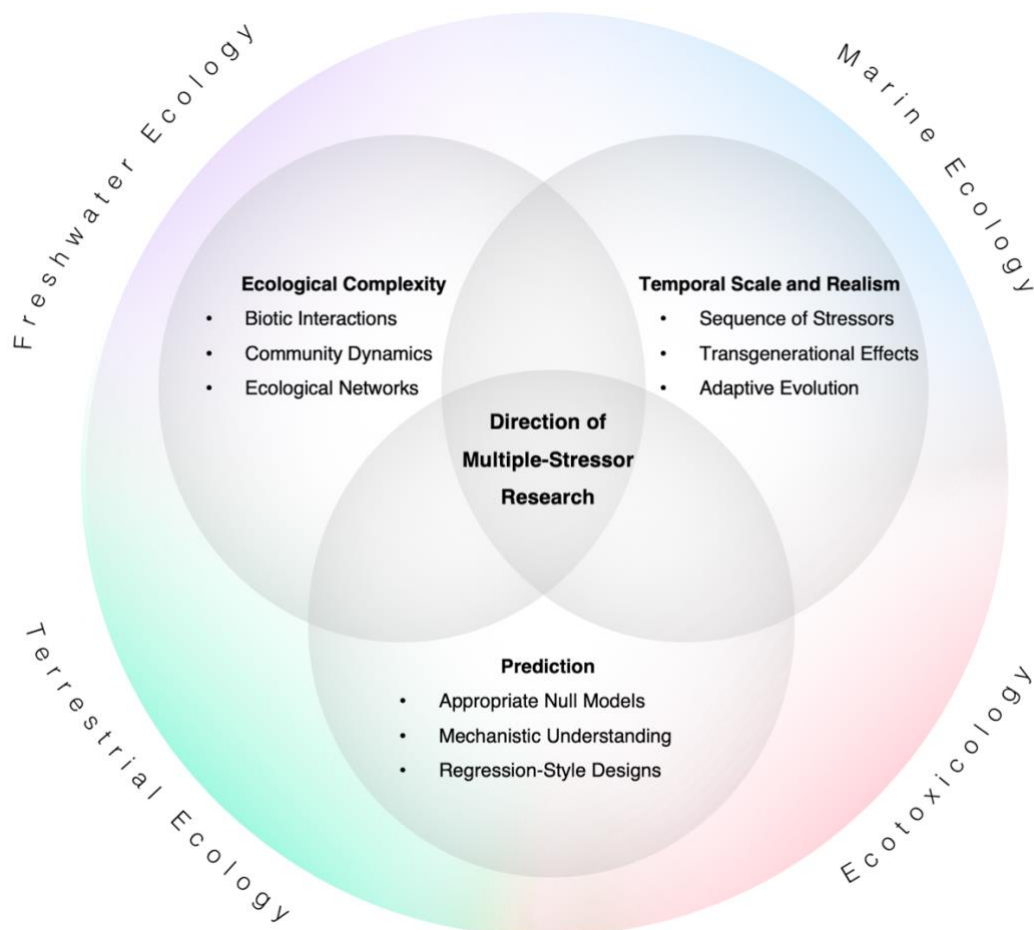
297

298 **4.1 Ecological Complexity**

299 Multiple-stressor research needs to shift its focus towards higher levels of biological
 300 organization as ecosystem managers are primarily interested in the effect of stressors on
 301 communities and ecosystems (25, 51). Researchers have called for this increase in ecological
 302 complexity in freshwater (52, 53), marine (31, 54) and terrestrial (26) ecology as well as in
 303 ecotoxicology (55). A key question is to what extent species interactions explain statistical
 304 interactions between stressors themselves at the community and ecosystem level.

305

306



307

308 **Figure 3:** An integrative conceptual framework of research goals shared by all disciplines,
 309 highlighting the future direction of multiple-stressor research.

310

311 Several different approaches have been taken to evaluate the roles of species interactions and
 312 level of organisation in responses to multiple stressors. For example, in their review of 171
 313 multiple-stressor studies in marine and coastal ecosystems, Crain *et al.* (3) found that
 314 synergism was most common in population-level studies, but antagonism was most common
 315 in community-level studies. Similarly, Côté *et al.* (29) found that synergism became less
 316 common as biological scale increased in their quantitative review across disciplines.
 317 However, Jackson *et al.* (5) found no significant difference in the frequencies of interaction
 318 types at the different biological levels in their review of freshwater studies. Moving beyond
 319 this “vote-counting” approach, researchers have conducted specific experimental (56, 57) and

320 modelling (58, 59) research on this topic. For example, Galic *et al.* (58) used population
321 models to show that hypothetical stressors with different modes of action primarily interacted
322 antagonistically at the individual level but synergistically at the population level.

323

324 Some theory has been developed to predict the impacts of multiple stressors at higher levels
325 of organisation (25, 51). De Laender (51) showed how competition for common resources can
326 lead to both synergistic and antagonistic effects of multiple stressors on species richness. In
327 general, the combined effect of multiple stressors can be amplified at the community level
328 when stressors act on influential groups such as keystone species or ecosystem engineers (41,
329 60). Likewise, biotic interactions can mitigate the effect of stressors (e.g., 61, 62). For
330 example, a modelling study showed that negative interactions among species (e.g.,
331 competition) increased the net negative effects of external stressors on community-level
332 properties while positive species interactions (e.g. mutualism) lessened negative impacts (40).

333

334 Interspecific interactions may themselves change after exposure to stressors. For example,
335 stressors may influence resource competition (63) and may change the susceptibility of hosts
336 to pathogens and parasites (64, 65). Equally, stressors can alter the trophic relationships of
337 species (56, 66). Schrama *et al.* (67) applied multiple pesticides to pond mesocosms and used
338 stable isotope analysis to show that these stressors and their interactions modified the flow of
339 energy through the food web by inducing shifts in trophic links. Furthermore, biotic
340 interactions can themselves act as stressors and consequently interact with other stressors. For
341 instance, the interactions between climate change and ungulate herbivory modulate effects on
342 forest ecosystems (e.g., 68).

343

344 The importance of biotic interactions in understanding the effects of stressors highlights the
345 need for an ecological network approach towards multiple-stressor studies (69).
346 Developments in technologies such as DNA metabarcoding and stable isotope analysis are
347 improving our ability to detect and quantify biotic interactions (70, 71). With these
348 technologies, multiple-stressor researchers will be able to clarify to what degree biotic
349 interactions mediate the statistical interactions between stressors and to ultimately determine
350 how we understand and predict the effects of multiple stressors.

351

352 **4.2 Temporal Scale and Realism**

353 The combined effects of stressors depend on various, largely overlooked, factors related to
354 different time scales (29, 30). At the time scale within one generation, several temporal
355 factors have been identified that may determine responses to multiple stressors. First, the
356 sequence of exposure to stressors may be crucial. For example, the order of exposure of two
357 toxicants determined their combined effect on *Gammarus pulex* (72). Here, if species'
358 responses to stressors are negatively correlated, sequence of exposure may be more important
359 than if their responses are positively correlated (23). Specifically, if paired stressors each
360 exert a different effect on species, order of exposure may be more important than if their
361 effects are redundant. Second, the time interval between stressors may influence their
362 combined impact. Gunderson *et al.* (30) developed a conceptual framework that predicts the
363 interaction type between sequential exposure to two stressors to be additive when the time
364 interval between exposure is long, but synergistic when time interval is short. Notably, there
365 may also be a time lag between the simultaneous exposure to two stressors and the synergistic
366 effect. For example, combined exposure to both warming and a pollutant in the larval stage of
367 a damselfly generated a strong synergistic effect across metamorphosis by reducing adult
368 lifespan (73). Interactions between stressors can also depend on the developmental stage of an

369 organism. Indeed, interactive effects may change, and even reverse, throughout ontogeny.
370 Przeslawski *et al.* (45) showed in a meta-analysis of marine organisms that the combination of
371 thermal and salinity stress was more likely to be synergistic for embryonic than for larval life
372 stages, yet the opposite pattern occurred between thermal and pH stress. Few studies,
373 however, have tested variation in interactions across developmental stages within the same
374 species (but see: 74).

375

376 At the time scale of a few generations, little is known about how the interaction type between
377 stressors in offspring depends on the exposure of the parents to those stressors. As a rare
378 example, a synergistic interaction between warming and a pollutant was detected in the
379 mosquito *Culex pipiens* both in the parents and in the offspring of parents exposed to none or
380 a single stressor. By contrast, an additive effect was present in the offspring of parents
381 exposed to both stressors simultaneously, because in this condition the pesticide was already
382 more lethal at the lower temperature (75). At the time scale of tens of generations, the
383 evolution of adaptation to a stressor may shape tolerance to subsequent stressors because of
384 pleiotropic effects where the same set of genes contributes to tolerance against different
385 stressors. This may cause co-tolerance where the acquisition of genetic adaptation to one
386 stressor increases tolerance to another (76), which is likely as genetic mechanisms of
387 tolerance to stressors are often conserved (77). Yet, pleiotropic effects may also be
388 antagonistic resulting in adaptive evolution to one stressor actually reducing tolerance to a
389 second (78). It is important to note that adaptation (79) and acclimatization (80) to a stressor
390 may come at a fitness cost. Finally, at a time scale of hundreds of generations, evolution of
391 thermal tolerance of a damselfly most likely resulted in the synergistic interaction between
392 warming and a pollutant in high-latitude populations to become additive in low-latitude
393 populations (81).

394

395 Experiments should attempt to use realistic timing of stressors over meaningful timescales
396 (e.g., 82), but this can be impractical, and observational studies may need to fill this gap (83).
397 Furthermore, certain stressors, for example nitrogen deposition (84), accumulate over time,
398 which can delay ecological effects and further complicate multiple-stressor predictions.
399 Importantly, the background variation under ambient conditions needs to be considered: a
400 recent example from plant communities showed that ambient changes may actually outweigh
401 the impact of stressors over time (85). Understanding if and how interactions between
402 stressors can change over time is a goal shared by all disciplines.

403

404 **4.3 Prediction**

405 The ultimate goal of multiple-stressor research is prediction of the combined effect of
406 stressors. This would allow for the incorporation of multiple-stressor research into a risk
407 assessment framework (86). Over the past twenty years a vast amount of research has been
408 conducted to test the effects of specific combinations of stressors on specific response
409 variables. However, very few, if any, general patterns have emerged from meta-analyses (3-6,
410 17, 18). This approach to studying multiple stressors, calculating proportions of interaction
411 types across different environments, conditions and responses, does not improve our
412 predictive capacity of multiple stressors for a variety of reasons, including the existence of a
413 publication bias towards synergism (29). Furthermore, the results are often context-dependent
414 (41) and prevent generalization, apart from the fact that non-additivity between stressors is
415 common.

416

417 To advance research of multiple stressors, there is a need to move beyond comparing
418 proportions of interaction types and shift focus towards improving our mechanistic

419 understanding of stressor interactions. A shift towards regression-style experimental designs
420 would enhance our understanding of stressor-response relationships, thus increasing our
421 ability to predict threshold responses (87, 88). When predicting the combined effects of
422 multiple stressors, it is important to consider both the modes of action of stressors and their
423 interactions. For example, the similarity or dissimilarity of stressors' modes of action may
424 reveal important information about how they may interact (8, 23). Equally, according to Boyd
425 and Brown (31), there are multiple modes of interaction between stressors at the physico-
426 chemical, organismal, and ecosystem levels. This concept, of statistical interactions between
427 stressors occurring as a result of interactions between stressors at different scales, is gaining
428 more attention (e.g., 41, 54).

429

430 A major issues that needs to be resolved is the use of null models. The additive null model has
431 been widely used, but also widely criticized for being inappropriate in many scenarios (29).
432 For example, it is biased towards antagonism when metrics with a fixed boundary, such as
433 mortality, are used as response variables (8, 17). Many null models can be useful for multiple-
434 stressor researchers, including both established models from the ecotoxicological literature
435 and new developments such as the *Stress Addition Model* (24) and the *Compositional Null*
436 *Model* (25). Researchers need to be aware of the different null models available and their
437 association with statistical tests (55). A recent framework for a mechanistic basis to null
438 model selection aims to facilitate a shift towards a more predictive approach (27). The
439 objective is to use null models that accurately predict the combined effects of stressors.
440 "Ecological surprises" arise when our null models are wrong, and researchers are unable to
441 explain why. Debate over null models and the emerging publications have almost entirely
442 bypassed the terrestrial global change research community, even though such considerations
443 could influence the interpretation of some of their findings considerably. Predicting the

444 impacts of multiple stressors is a common goal shared by all disciplines, and achieving this
445 goal is vital for the sustainable management of resources and for the conservation of
446 biodiversity and ecosystem services.

447

448 **5. Conclusions**

449 Multiple-stressor researchers from different disciplines are clearly separated. This was
450 identified during our cross-disciplinary review and was confirmed using bibliometric analysis.

451 The use of different terminology for predictor variables and for interactions between those
452 variables has reinforced this separation. Common terminology, or at least awareness of the
453 different terms in online searches and meta-analyses, would greatly enhance cross-
454 disciplinary collaboration and would encourage the integration of multiple-stressor research
455 into mainstream ecology. In fact, our conclusion that researchers should be aware of
456 terminology from different disciplines applies to all ecological research.

457

458 In future work, researchers should consider multiple-stressor literature from other disciplines
459 for guidance on methods and analyses. Authors of primary research should include multiple
460 terms in their keyword section to enhance the visibility of their research. However, limits on
461 the number of keywords in journals may incentivize authors to only use keywords relevant to
462 their own discipline. Meta-analyses of the multiple-stressor literature should consider the
463 broader range of terminology identified in this review (see common glossary: Table 2) and,
464 where possible, be repeated to include relevant but previously missed studies. Multiple-
465 stressor research is moving forward with all disciplines converging towards the same
466 common goals, and the time is ripe for a unified approach. Division between ecosystem types
467 and disciplines is largely a human creation. Species and stressors cross these borders, and so
468 should the scientists who study them.

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472

473

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478

479

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