Electronic Supplementary Material

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

Authors: James A. Orr, Rolf D. Vinebrooke, Michelle C. Jackson, Kristy J. Kroeker, Rebecca L. Kordas, Chrystal Mantyka-Pringle, Paul J. Van den Brink, Frederik De Laender, Robby Stoks, Martin Holmstrup, Christoph D. Matthaei, Wendy A. Monk, Marcin R. Penk, Sebastian Leuzinger, Ralf B. Schäfer, Jeremy J. Piggott

Journal: Proceedings of the Royal Society B

Article DOI: 10.1098/rspb.2020.0421

SM1: Web of Science Search

- **SM2:** Bibliometric Analysis Methods
- SM3: Citation Network with Colours based on Clusters
- SM4: Citation Networks Where the Size of Nodes is Based on the Number of Citations
- SM5: Larger Citation Networks with Lower Citation Threshold

SM6: Heat Map of Disciplines in Each Cluster

- SM7: Terms in the Term Network
- **SM8:** Cross-Discipline Comparison

SM1: Web of Science Search

A search was conducted on the 30th of June 2019 on the *ISI Web of Knowledge* database (https://apps.webofknowledge.com) to collect publications from the multiple-stressor literature using the following search terms:

Title = ("multiple stress*" OR "stressors" OR "global change factors" OR "environmental factors" OR "global change drivers" OR "multiple drivers" OR "synerg*" OR "amplify*" OR "antagon*" OR "dampen*" OR "additive" OR "interactive effects" OR "multifactor" OR "nitrogen and phosphorus limitation" OR "multiple limiting resources" OR "nutrient co-limitation" OR "global change experiments")

AND

Topic = ("multiple stress*" OR "stressors" OR "global change factors" OR "global change drivers" OR "multifactor" OR "cumulative effect*" OR "net effect*" OR "combined effect*" OR "interacting" OR " nitrogen and phosphorus limitation " OR "multiple limiting resources" OR "nutrient co-limitation" OR "global change experiments") AND

Web of Science Category = ("Ecology" OR "Toxicology" OR "Environmental Sciences" OR "Plant Sciences" OR "Zoology" OR "Marine Freshwater Biology" OR "Limnology" OR "Oceanography" OR "Multidisciplinary Sciences")

AND

Year Published = (1999-2019)

The search returned 2,268 results, which were extracted as full record .txt files.

SM2: Bibliometric Analysis Methods

Bibliometric analysis was conducted using *VOSviewer* version 1.6.11 (1). *VOSviewer* is a piece of software used for visualization and analysis of networks, primarily constructed using bibliometric data.

(i) Citation Network

In order to allow for readability of the networks, out of the 2268 results, only the top 300 publications based on the number of citations were used to construct initial citation networks. Due to a bias towards marine and freshwater publications in this initial citation network, the 25 next most highly cited terrestrial and ecotoxicological publications were added to the network so that all disciplines were similar in number. The largest connected network (150 publications) from this pool of 350 publications was selected so that irrelevant papers (i.e. publications that were not from the multiple stressor literature) were ignored. Citation networks of the 150 connected publications were constructed with the following settings in *VOSviewer*:

- Bibliometric analysis = Citation Analysis
- Unit of analysis = Documents
- *Counting methods = Full counting*
- *Minimum cluster size* = 15 (*Total number of publications divided by 10*)

Although these 150 publications are the most "influential" or cited publications in the multiple stressor literature and there is a roughly equal representation of publications from each of the four disciplines, to ensure that our networks were not biased we create four more networks comprised of the top 500, 1000, 1500 and 2000 publications based on the number of publications. The same settings were used as above except the minimum cluster size was modified so that there was always the same number of clusters in each network to allow for comparisons to be made.

(ii) Term Network

Using the same 150 papers that comprised the citation networks in Figure 1, term networks were constructed, again using *VOSviewer*. Terms were extracted from the title and abstract fields. Structured abstract labels and copyright statements were ignored. Terms that occurred at least 10 times were included, resulting in a network comprised of 161 terms. The following settings were used in *VOSviewer*:

- *Counting methods = Full counting*
- Normalization = Association Strength
- *Maximum number of links* = 2500 (to enhance visibility)

(iii) 150 publications used for citation and term networks, ordered by total citations

| Name | Discipline | Links | Citations | Cluster | Document Title | |
|-------------------|------------|-------|-----------|---------|--|--|
| in Network | | | (WoS) | | | |
| elser (2007) | general | 11 | 1683 | 1 | Global analysis of nitrogen and phosphorus limitation of primary | |
| | | | | | producers in freshwater, marine and terrestrial ecosystems | |
| brook (2008) | general | 4 | 817 | 1 | Synergies among extinction drivers under global change | |
| crain (2008) | marine | 31 | 773 | 5 | Interactive and cumulative effects of multiple human stressors in | |
| | | | | | marine systems | |
| bopp (2013) | marine | 3 | 455 | 3 | Multiple stressors of ocean ecosystems in the 21st century: | |
| | | | | | projections with CMIP5 models | |
| strayer (2010) | fresh | 1 | 437 | 2 | Alien species in fresh waters: ecological effects, interactions with | |
| | | | | | other stressors, and prospects for the future | |
| didham (2007) | general | 4 | 436 | 1 | Interactive effects of habitat modification and species invasion on | |
| | | | | | native species decline | |
| folt (1999) | general | 28 | 392 | 5 | Synergism and antagonism among multiple stressors | |
| hughes (1999) | marine | 7 | 377 | 4 | Multiple stressors on coral reefs: A long-term perspective | |
| darling (2008) | general | 26 | 352 | 5 | Quantifying the evidence for ecological synergies | |
| vinebrooke (2004) | general | 24 | 342 | 1 | Impacts of multiple stressors on biodiversity and ecosystem | |
| | | | | | functioning: the role of species co-tolerance | |
| harpole (2011) | general | 8 | 337 | 1 | Nutrient co-limitation of primary producer communities | |
| holmstrup (2010) | ecotox | 18 | 329 | 4 | Interactions between effects of environmental chemicals and natural | |
| | | | | | stressors: A review | |
| heugens (2001) | ecotox | 6 | 310 | 4 | A review of the effects of multiple stressors on aquatic organisms | |
| | | | | | and analysis of uncertainty factors for use in risk assessment | |
| klein (2004) | terr | 1 | 246 | 3 | Experimental warming causes large and rapid species loss, | |
| | | | | | dampened by simulated grazing, on the Tibetan Plateau | |
| ormerod (2010) | fresh | 16 | 245 | 2 | Multiple stressors in freshwater ecosystems | |
| statzner (2010) | fresh | 8 | 204 | 2 | Can biological invertebrate traits resolve effects of multiple | |
| | | | | | stressors on running water ecosystems? | |
| sokolova (2008) | ecotox | 6 | 187 | 3 | Interactive effects of metal pollution and temperature on | |
| | | | | | metabolism in aquatic ectotherms: implications of global climate | |
| | | | | | change | |
| leuzinger (2011) | terr | 5 | 185 | 1 | Do global change experiments overestimate impacts on terrestrial | |
| | | | | | ecosystems? | |
| strayer (2008) | fresh | 2 | 183 | 2 | Freshwater Mussel Ecology: A Multifactor Approach to | |
| | | | | | Distribution and Abundance | |
| dieleman (2012) | terr | 6 | 180 | 1 | Simple additive effects are rare: a quantitative review of plant | |
| | | | | | biomass and soil process responses to combined manipulations of | |
| | | | | | CO ₂ and temperature | |
| luo (2008) | terr | 7 | 180 | 1 | Modeled interactive effects of precipitation, temperature, and [CO2] | |
| | | | | | on ecosystem carbon and water dynamics in different climatic zones | |

| zavaleta (2003) | terr | 4 | 179 | 3 | Additive effects of simulated climate changes, elevated CO ₂ , and | |
|--------------------|---------|----|-----|---|---|--|
| | | | | | nitrogen deposition on grassland diversity | |
| paerl (2006) | marine | 1 | 177 | 6 | Assessing and managing nutrient-enhanced eutrophication in | |
| | | | | | estuarine and coastal waters: Interactive effects of human and | |
| | | | | | climatic perturbations | |
| tockner (2010) | fresh | 8 | 173 | 6 | Multiple stressors in coupled river-floodplain ecosystems | |
| ollinger (2002) | terr | 1 | 167 | 1 | Interactive effects of nitrogen deposition, tropospheric ozone, | |
| | | | | | elevated CO2 and land use history on the carbon dynamics of | |
| | | | | | northern hardwood forests | |
| russell (2009) | marine | 3 | 163 | 5 | Synergistic effects of climate change and local stressors: CO2 and | |
| | | | | | nutrient-driven change in subtidal rocky habitats | |
| townsend (2008) | fresh | 14 | 162 | 6 | Individual and combined responses of stream ecosystems to | |
| | | | | | multiple stressors | |
| harvey (2013) | marine | 8 | 158 | 5 | Meta-analysis reveals complex marine biological responses to the | |
| | | | | | interactive effects of ocean acidification and warming | |
| allan (2013) | fresh | 2 | 156 | 5 | Joint analysis of stressors and ecosystem services to enhance | |
| | | | | | restoration effectiveness | |
| sokolova (2013) | ecotox | 8 | 153 | 3 | Energy-Limited Tolerance to Stress as a Conceptual Framework to | |
| | | | | | Integrate the Effects of Multiple Stressors | |
| coors (2008) | ecotox | 10 | 147 | 4 | Synergistic, antagonistic and additive effects of multiple stressors: | |
| | | | | | predation threat, parasitism and pesticide exposure in Daphnia | |
| | | | | | magna | |
| jackson (2016) | fresh | 15 | 147 | 2 | Net effects of multiple stressors in freshwater ecosystems: a meta- | |
| | | | | | analysis | |
| matthaei (2010) | fresh | 8 | 147 | 6 | Multiple stressors in agricultural streams: interactions among | |
| | | | | | sediment addition, nutrient enrichment and water abstraction | |
| davidson (2004) | terr | 1 | 141 | 1 | Nitrogen and phosphorus limitation of biomass growth in a tropical | |
| | | | | | secondary forest | |
| christensen (2006) | fresh | 16 | 138 | 3 | Multiple anthropogenic stressors cause ecological surprises in | |
| | | | | | boreal lakes | |
| carilli (2009) | marine | 4 | 134 | 2 | Local Stressors Reduce Coral Resilience to Bleaching | |
| hecky (2010) | fresh | 2 | 134 | 2 | Multiple stressors cause rapid ecosystem change in Lake Victoria | |
| ban (2014) | marine | 19 | 133 | 2 | Evidence for multiple stressor interactions and effects on coral reefs | |
| boone (2003) | general | 3 | 128 | 5 | Interactions of an insecticide, herbicide, and natural stressors in | |
| | | | | | amphibian community mesocosms | |
| thurber (2008) | marine | 2 | 127 | 2 | Metagenomic analysis indicates that stressors induce production of | |
| | | | | | herpes-like viruses in the coral Porites compressa | |
| sih (2004) | general | 3 | 123 | 3 | Two stressors are far deadlier than one | |
| ferreira (2011) | fresh | 2 | 121 | 5 | Synergistic effects of water temperature and dissolved nutrients on | |
| | | | | | litter decomposition and associated fungi | |
| gunderson (2016) | marine | 15 | 121 | 3 | Multiple Stressors in a Changing World: The Need for an Improved | |
| | | | | | Perspective on Physiological Responses to the Dynamic Marine | |
| | | | | | Environment | |
| | 1 | | 1 | 1 | | |

| piggott (2015) | general | 15 | 121 | 2 | Reconceptualizing synergism and antagonism among multiple | |
|--------------------|---------|----|-----|---|---|--|
| | | | | | stressors | |
| moe (2013) | ecotox | 3 | 118 | 4 | Combined and interactive effects of global climate change and | |
| | | | | | toxicants on populations and communities | |
| adams (2005) | marine | 5 | 117 | 6 | Assessing cause and effect of multiple stressors on marine systems | |
| przeslawski (2015) | marine | 12 | 117 | 5 | A review and meta-analysis of the effects of multiple abiotic | |
| | | | | | stressors on marine embryos and larvae | |
| tian (2011) | terr | 2 | 116 | 1 | China's terrestrial carbon balance: Contributions from multiple | |
| | | | | | global change factors | |
| boone (2007) | general | 3 | 115 | 5 | Multiple stressors in amphibian communities: Effects of chemical | |
| | | | | | contamination, bullfrogs, and fish | |
| hooper (2013) | ecotox | 3 | 109 | 4 | Interactions between chemical and climate stressors: A role for | |
| | | | | | mechanistic toxicology in assessing climate change risks | |
| mikkelsen (2008) | terr | 4 | 104 | 1 | Experimental design of multifactor climate change experiments | |
| | | | | | with elevated CO ₂ , warming and drought: the CLIMAITE project | |
| hering (2015) | fresh | 3 | 103 | 2 | Managing aquatic ecosystems and water resources under multiple | |
| | | | | | stress - An introduction to the MARS project | |
| cote (2016) | general | 16 | 101 | 1 | Interactions among ecosystem stressors and their importance in | |
| | | | | | conservation | |
| boyd (2015) | marine | 5 | 100 | 3 | Biological ramifications of climate-change-mediated oceanic multi- | |
| | | | | | stressors | |
| lenihan (1999) | marine | 3 | 96 | 6 | The influence of multiple environmental stressors on susceptibility | |
| | | | | | to parasites: An experimental determination with oysters | |
| wagenhoff (2011) | fresh | 9 | 96 | 6 | Subsidy-stress and multiple-stressor effects along gradients of | |
| | | | | | deposited fine sediment and dissolved nutrients in a regional set of | |
| | | | | | streams and rivers | |
| aufauvre (2012) | ecotox | 1 | 94 | 4 | Parasite-insecticide interactions: a case study of Nosema ceranae | |
| | | | | | and fipronil synergy on honeybee | |
| porter (1999) | marine | 4 | 94 | 2 | The effect of multiple stressors on the Florida Keys coral reef | |
| | | | | | ecosystem: A landscape hypothesis and a physiological test | |
| darling (2013) | marine | 3 | 91 | 1 | Life histories predict coral community disassembly under multiple | |
| | | | | | stressors | |
| kawai (2007) | marine | 2 | 91 | 5 | Testing the facilitation-competition paradigm under the stress- | |
| | | | | | gradient hypothesis: decoupling multiple stress factors | |
| abell (2010) | fresh | 1 | 89 | 1 | Nitrogen and Phosphorus Limitation of Phytoplankton Growth in | |
| | | | | | New Zealand Lakes: Implications for Eutrophication Control | |
| kuntz (2005) | marine | 4 | 89 | 2 | Pathologies and mortality rates caused by organic carbon and | |
| | | | | | nutrient stressors in three Caribbean coral species | |
| przeslawski (2005) | marine | 10 | 89 | 5 | Synergistic effects associated with climate change and the | |
| | | | | | development of rocky shore molluscs | |
| smol (2010) | fresh | 1 | 88 | 2 | The power of the past: using sediments to track the effects of | |
| | | | | | multiple stressors on lake ecosystems | |
| todgham (2013) | general | 8 | 88 | 3 | Physiological Responses to Shifts in Multiple Environmental | |
| | | | | | Stressors: Relevance in a Changing World | |

| zhou (2006a) | terr | 1 | 87 | 1 | Main and interactive effects of warming, clipping, and doubled | |
|-------------------|---------|----|----|---|--|--|
| | | | | | precipitation on soil CO2 efflux in a grassland ecosystem | |
| brown (2013) | marine | 9 | 86 | 2 | Managing for Interactions between Local and Global Stressors of | |
| | | | | | Ecosystems | |
| rohr (2004) | general | 2 | 86 | 5 | Multiple stressors and salamanders: Effects of an herbicide, food | |
| | | | | | limitation, and hydroperiod | |
| stendera (2012) | fresh | 3 | 86 | 2 | Drivers and stressors of freshwater biodiversity patterns across | |
| | | | | | different ecosystems and scales: a review | |
| gobler (2014) | marine | 3 | 85 | 3 | Hypoxia and Acidification Have Additive and Synergistic Negative | |
| | | | | | Effects on the Growth, Survival, and Metamorphosis of Early Life | |
| | | | | | Stage Bivalves | |
| navarro-ortega | fresh | 4 | 80 | 2 | Managing the effects of multiple stressors on aquatic ecosystems | |
| (2015) | | | | | under water scarcity. The GLOBAQUA project | |
| stone (2001) | ecotox | 1 | 80 | 4 | Time to death response in carabid beetles exposed to multiple | |
| | | | | | stressors along a gradient of heavy metal pollution | |
| alvarez-clare | terr | 3 | 79 | 1 | A direct test of nitrogen and phosphorus limitation to net primary | |
| (2013) | | | | | productivity in a lowland tropical wet forest | |
| strain (2014) | marine | 10 | 79 | 5 | Identifying the interacting roles of stressors in driving the global | |
| | | | | | loss of canopy-forming to mat-forming algae in marine ecosystems | |
| davidson (2007) | general | 1 | 77 | 6 | Multiple stressors and amphibian declines: Dual impacts of | |
| | | | | | pesticides and fish on yellow-legged frogs | |
| cottingham (1999) | fresh | 3 | 75 | 6 | Nutrients and zooplankton as multiple stressors of phytoplankton | |
| | | | | | communities: Evidence from size structure | |
| piggott (2012) | fresh | 9 | 75 | 5 | Multiple Stressors in Agricultural Streams: A Mesocosm Study of | |
| | | | | | Interactions among Raised Water Temperature, Sediment Additio | |
| | | | | | and Nutrient Enrichment | |
| yan (2008) | fresh | 3 | 75 | 4 | Long-term trends in zooplankton of Dorset, Ontario, lakes: the | |
| | | | | | probable interactive effects of changes in pH, total phosphorus, | |
| | | | | | dissolved organic carbon, and predators | |
| laskowski (2010) | ecotox | 7 | 74 | 4 | Interactions between toxic chemicals and natural environmental | |
| | | | | | factors - A meta-analysis and case studies | |
| breitburg (2015) | marine | 5 | 72 | 3 | And on Top of All That Coping with Ocean Acidification in the | |
| | | | | | Midst of Many Stressors | |
| burton (2010) | ecotox | 7 | 71 | 2 | Assessing contaminated sediments in the context of multiple | |
| | | | | | stressors | |
| heugens (2006) | ecotox | 12 | 71 | 4 | Population growth of Daphnia magna under multiple stress | |
| | | | | | conditions: Joint effects of temperature, food, and cadmium | |
| harpole (2016) | terr | 2 | 70 | 1 | Addition of multiple limiting resources reduces grassland diversity | |
| heathwaite (2010) | fresh | 3 | 68 | 2 | Multiple stressors on water availability at global to catchment | |
| | | | | | scales: understanding human impact on nutrient cycles to protect | |
| | | | | | water quality and water availability in the long term | |
| niu (2009) | terr | 2 | 68 | 1 | Non-Additive Effects of Water and Nitrogen Addition on | |
| | | | | | Ecosystem Carbon Exchange in a Temperate Steppe | |

| cardoso (2008) | marine | 3 | 67 | 6 | The impact of extreme flooding events and anthropogenic stressors | |
|------------------|---------|----|----|---|--|--|
| | | | | | on the macrobenthic communities' dynamics | |
| seo (2006) | ecotox | 1 | 67 | 3 | Environmental stressors (salinity, heavy metals, H2O2) modulate | |
| | | | | | expression of glutathione reductase (GR) gene from the intertidal | |
| | | | | | copepod Tigriopus japonicus | |
| lirman (2007) | marine | 1 | 66 | 2 | Is proximity to land-based sources of coral stressors an appropriate | |
| | | | | | measure of risk to coral reefs? An example from the Florida Reef | |
| | | | | | Tract | |
| altshuler (2011) | ecotox | 10 | 65 | 4 | An Integrated Multi-Disciplinary Approach for Studying Multiple | |
| | | | | | Stressors in Freshwater Ecosystems: <i>Daphnia</i> as a Model Organism | |
| babu (2001) | ecotox | 1 | 64 | 2 | Synergistic effects of a photooxidized polycyclic aromatic | |
| | | | | | hydrocarbon and copper on photosynthesis and plant growth: | |
| | | | | | Evidence that in vivo formation of reactive oxygen species is a | |
| | | | | | mechanism of copper toxicity | |
| downes (2010) | fresh | 4 | 64 | 2 | Back to the future: little-used tools and principles of scientific | |
| | | | | | inference can help disentangle effects of multiple stressors on | |
| | | | | | freshwater ecosystems | |
| chen (2004) | ecotox | 4 | 63 | 6 | Multiple stress effects of Vision (R) herbicide, pH, and food on | |
| () | | | | - | zooplankton and larval amphibian species from forest wetlands | |
| van (2004) | fresh | 3 | 63 | 4 | Recovery of copenod but not cladoceran zooplankton from severe | |
| Jun (2001) | neon | 5 | 00 | | and chronic effects of multiple stressors | |
| lu (2012) | terr | 3 | 62 | 1 | Effect of nitrogen deposition on China's terrestrial carbon uptake in | |
| iu (2012) | | 5 | 02 | 1 | the context of multifactor environmental changes | |
| mcbryan (2013) | general | 5 | 62 | 3 | Responses to Temperature and Hypoxia as Interacting Stressors in | |
| meoryan (2013) | general | 5 | 02 | 5 | Fish: Implications for Adaptation to Environmental Change | |
| bancroft (2008) | general | 3 | 60 | 3 | A mata-analysis of the affacts of ultraviolat R radiation and its | |
| buildfort (2000) | general | 5 | 00 | 5 | synergistic interactions with nH contaminants and disease on | |
| | | | | | amphibian survival | |
| noges (2016) | general | 11 | 60 | 2 | Quantified biotic and abiotic responses to multiple stress in | |
| 10203 (2010) | general | 11 | 00 | 2 | freshwater marine and ground waters | |
| segner (2014) | general | 15 | 59 | 4 | Assessing the Impact of Multiple Stressors on Aquatic Biota: The | |
| segner (2014) | general | 15 | 57 | + | Recentor's Side Matters | |
| carilli (2010) | marine | 3 | 58 | 2 | Century-scale records of coral growth rates indicate that local | |
| carini (2010) | marme | 5 | 50 | 2 | stressors reduce coral thermal tolerance threshold | |
| atawabarban | marina | 4 | 57 | 2 | Climate change impacts on corel reefs: Supergies with local effects | |
| (2013) | marme | 4 | 57 | 2 | possibilities for acclimation and management implications | |
| (2013) | tam | 1 | 56 | 1 | Competitive interactions between two meedow eroses under | |
| venternik (2010) | terr | 1 | 50 | | nitrogen and phosphorus limitation | |
| (1 (2010) | C 1 | 1 | 55 | 2 | | |
| grantnam (2010) | Iresh | 1 | 22 | 2 | Chimatic influences and anthropogenic stressors: an integrated | |
| | | | | | Iramework for streamflow management in Mediterranean-climate | |
| (2001) | | | | | | |
| gunn (2001) | tresh | 1 | 55 | 4 | Use of water clarify to monitor the effects of climate change and | |
| | | | | | other stressors on oligotrophic lakes | |

| heckmann (2012) | general | 1 | 55 | 1 | Interactive effects of body-size structure and adaptive foraging on |
|--------------------|---------|----|----|---|---|
| | | | | | food-web stability |
| bernez (2004) | fresh | 1 | 54 | 2 | Combined effects of environmental factors and regulation on |
| | | | | | macrophyte vegetation along three rivers in western France |
| rohr (2013) | general | 1 | 54 | 5 | Climate Change, Multiple Stressors, and the Decline of Ectotherms |
| selsted (2012) | terr | 4 | 53 | 1 | Soil respiration is stimulated by elevated CO ₂ and reduced by |
| | | | | | summer drought: three years of measurements in a multifactor |
| | | | | | ecosystem manipulation experiment in a temperate heathland |
| | | | | | (CLIMAITE) |
| adams (2003) | general | 1 | 52 | 6 | Establishing causality between environmental stressors and effects |
| | | | | | on aquatic ecosystems |
| lenihan (2003) | marine | 1 | 52 | 6 | Variation in marine benthic community composition allows |
| | | | | | discrimination of multiple stressors |
| piggott (2015a) | fresh | 8 | 52 | 6 | Climate warming and agricultural stressors interact to determine |
| | | | | | stream periphyton community composition |
| liess (2016) | ecotox | 3 | 51 | 4 | Predicting the synergy of multiple stress effects |
| thrush (2008) | ecotox | 4 | 51 | 6 | Multiple stressor effects identified from species abundance |
| | | | | | distributions: Interactions between urban contaminants and species |
| | | | | | habitat relationships |
| fredersdorf (2009) | marine | 1 | 50 | 3 | Interactive effects of radiation, temperature and salinity on different |
| | | | | | life history stages of the Arctic kelp Alaria esculenta |
| | | | | | (Phaeophyceae) |
| mueller (2016) | terr | 2 | 49 | 1 | Impacts of warming and elevated CO2 on a semi-arid grassland are |
| | | | | | non-additive, shift with precipitation, and reverse over time |
| hessen (2000) | fresh | 1 | 46 | 4 | UV radiation and low calcium as mutual stressors for Daphnia |
| kolzau (2014) | fresh | 2 | 46 | 1 | Seasonal Patterns of Nitrogen and Phosphorus Limitation in Four |
| | | | | | German Lakes and the Predictability of Limitation Status from |
| | | | | | Ambient Nutrient Concentrations |
| rose (2009) | marine | 1 | 46 | 3 | Synergistic effects of iron and temperature on Antarctic |
| | | | | | phytoplankton and microzooplankton assemblages |
| davis (2010) | fresh | 3 | 45 | 2 | Multiple stressors and regime shifts in shallow aquatic ecosystems |
| | | | | | in antipodean landscapes |
| dunne (2010) | marine | 3 | 45 | 2 | Synergy or antagonism-interactions between stressors on coral reefs |
| o'gorman (2012) | marine | 5 | 45 | 6 | Multiple anthropogenic stressors and the structural properties of |
| | | | | | food webs |
| schulte (2007) | marine | 1 | 45 | 3 | Responses to environmental stressors in an estuarine fish: |
| | | | | | Interacting stressors and the impacts of local adaptation |
| firth (2009) | marine | 4 | 44 | 3 | The influence of multiple environmental stressors on the limpet |
| | | | | | Cellana toreuma during the summer monsoon season in Hong Kong |
| merriam (2011) | fresh | 2 | 44 | 5 | Additive effects of mining and residential development on stream |
| | | | | | conditions in a central Appalachian watershed |
| piggott (2015b) | fresh | 12 | 44 | 6 | Climate warming and agricultural stressors interact to determine |
| | | | | | stream macroinvertebrate community dynamics |

| ren (2012) | terr | 3 | 44 | 1 | China's crop productivity and soil carbon storage as influenced by |
|------------------|--------|---|----|---|--|
| | | | | | multifactor global change |
| sundermann | fresh | 4 | 44 | 6 | Stressor prioritisation in riverine ecosystems: Which environmental |
| (2013) | | | | | factors shape benthic invertebrate assemblage metrics? |
| fagundez (2013) | terr | 3 | 43 | 1 | Heathlands confronting global change: drivers of biodiversity loss |
| | | | | | from past to future scenarios |
| fischer (2013) | ecotox | 9 | 43 | 4 | The toxicity of chemical pollutants in dynamic natural systems: The |
| | | | | | challenge of integrating environmental factors and biological |
| | | | | | complexity |
| albert (2011) | terr | 3 | 42 | 1 | Interactive effects of elevated CO2, warming, and drought on |
| | | | | | photosynthesis of Deschampsia flexuosa in a temperate heath |
| | | | | | ecosystem |
| gergs (2013) | ecotox | 1 | 39 | 4 | Chemical and natural stressors combined: from cryptic effects to |
| | | | | | population extinction |
| zhou (2016) | terr | 9 | 39 | 1 | Interactive effects of global change factors on soil respiration and its |
| | | | | | components: a meta-analysis |
| bindesbol (2005) | ecotox | 4 | 37 | 4 | Stress synergy between environmentally realistic levels of copper |
| | | | | | and frost in the earthworm Dendrobaena octaedra |
| boone (2008) | ecotox | 2 | 37 | 5 | Examining the single and interactive effects of three insecticides on |
| | | | | | amphibian metamorphosis |
| chiogna (2016) | ecotox | 3 | 37 | 2 | A review of hydrological and chemical stressors in the Adige |
| | | | | | catchment and its ecological status |
| ivanina (2011) | ecotox | 3 | 37 | 3 | Interactive effects of cadmium and hypoxia on metabolic responses |
| | | | | | and bacterial loads of eastern oysters Crassostrea virginica Gmelin |
| Iokke (2013) | ecotox | 5 | 37 | 4 | Tools and perspectives for assessing chemical mixtures and multiple |
| | | | | | stressors |
| kelly (2010) | ecotox | 1 | 36 | 6 | Synergistic effects of glyphosate formulation and parasite infection |
| | | | | | on fish malformations and survival |
| hojer (2001) | ecotox | 4 | 35 | 4 | Stress synergy between drought and a common environmental |
| | | | | | contaminant: studies with the collembolan Folsomia candida |
| craine (2010) | terr | 2 | 34 | 1 | Plant nitrogen and phosphorus limitation in 98 North American |
| | | | | | grassland soils |
| janssens (2013) | ecotox | 4 | 34 | 3 | Synergistic effects between pesticide stress and predator cues: |
| | | | | | Conflicting results from life history and physiology in the damselfly |
| | | | | | Enallagma cyathigerum |
| binzer (2016) | terr | 2 | 33 | 1 | Interactive effects of warming, eutrophication and size structure: |
| | | | | | impacts on biodiversity and food-web structure |
| de sassi (2012) | terr | 2 | 33 | 1 | Plant-mediated and nonadditive effects of two global change drivers |
| | | | | | on an insect herbivore community |
| whitehead (2013) | ecotox | 3 | 32 | 3 | Interactions between Oil-Spill Pollutants and Natural Stressors Can |
| | | | | | Compound Ecotoxicological Effects |
| mcknight (2012) | ecotox | 2 | 30 | 6 | Integrated assessment of the impact of chemical stressors on surface |
| | | | | | water ecosystems |

| eder (2007) | ecotox | 1 | 29 | 4 | Pesticide and pathogen: Heat shock protein expression and | |
|----------------|--------|---|----|---|---|--|
| | | | | | acetylcholinesterase inhibition in juvenile Chinook salmon in | |
| | | | | | response to multiple stressors | |
| maestre (2009) | terr | 1 | 28 | 5 | On the relationship between abiotic stress and co-occurrence | |
| | | | | | patterns: an assessment at the community level using soil lichen | |
| | | | | | communities and multiple stress gradients | |
| turner (2009) | terr | 1 | 28 | 3 | Interactive effects of warming and increased nitrogen deposition on | |
| | | | | | 15N tracer retention in a temperate old field: seasonal trends | |
| metz (2013) | terr | 1 | 27 | 5 | Unexpected redwood mortality from synergies between wildfire and | |
| | | | | | an emerging infectious disease | |
| yue (2017) | terr | 7 | 27 | 1 | Effects of three global change drivers on terrestrial C:N:P | |
| | | | | | stoichiometry: a global synthesis | |
| davalos (2014) | terr | 5 | 26 | 1 | Demographic responses of rare forest plants to multiple stressors: | |
| | | | | | the role of deer, invasive species and nutrients | |

SM3: Citation Network with Colours based on Clusters

Citation network where the nodes represent publications and the links indicate the presence of a citation between connected publications. The size of the nodes represents the number of citations normalized by age. The distance between nodes is calculated using a citation analysis algorithm which determines the relatedness of items based on the number of times they cite each other. The colours of the nodes and their links represent the different clusters of publications.



SM4: Citation Networks Where the Size of Nodes is Based on the Number of Citations

Citation network where the size of the nodes represents the number of links a publication has in the network. The colours of the nodes and their links represent (A) the different clusters of publications or (B) the disciplines they belong to.



SM5: Larger Citation Networks with Lower Citation Threshold

Citation networks constructed using the top 500 (1), 1000 (2), 1500 (3) and 2000 (4) publications based on citations using citations normalized by age of publication (A) and number of links (B) to calculate size of node. Minimum cluster size was modified so that there was always the same number of clusters in each network to allow for comparisons to be made.









SM6: Heat Map of Disciplines in Each Cluster

(i) Methods

- 1. For each cluster in the citation network the number of publications from each discipline was extracted.
- 2. These data were then converted to the percentage of each discipline in each cluster.
- 3. Finally, a heat map was constructed in R 3.6.0 (2) using the *gplots* package (3).

| | Cluster 1 | Cluster 2 | Cluster 3 | Cluster 4 | Cluster 5 | Cluster 6 | | | |
|--------------------------|------------|------------|-----------|------------|-----------|-----------|--|--|--|
| Freshwater [34] | 5.9% [2] | 44.1% [15] | 2.9% [1] | 11.8% [4] | 11.8% [4] | 23.5% [8] | | | |
| Marine [34] | 2.9% [1] | 29.4% [10] | 26.5% [9] | 2.9% [1] | 20.6% [7] | 17.6% [6] | | | |
| Terrestrial [29] | 82.8% [24] | 0% [0] | 10.3% [3] | 0% [0] | 6.9% [2] | 0% [0] | | | |
| Ecotoxicology [31] | 0% [0] | 9.7% [3] | 19.4% [6] | 54.8% [17] | 3.2% [1] | 12.9% [4] | | | |
| General [22] | 31.8% [7] | 9.1% [2] | 18.2% [4] | 4.5% [1] | 27.3% [6] | 9.1% [2] | | | |
| Percentage of Discipline | | | | | | | | | |

Heat map where cells contains the percentage (and number – in square brackets) of publications from each discipline found in the six clusters from SM3. The colour ramp, from light to dark red, corresponds to the percentage of publications from each discipline.

SM7: Terms in the Term Network

Terms from the term network ranked in order of number of occurrences. Disciplines have been manually assigned.

| Term | Occurrences | Discipline | type | 42 | General |
|--------------------|-------------|------------|-----------------|----|---------------|
| effect | 387 | General | data | 41 | General |
| stressor | 298 | General | importance | 40 | General |
| response | 160 | General | plant | 40 | Terrestrial |
| interaction | 155 | General | evidence | 39 | General |
| study | 150 | General | nutrient | 39 | General |
| change | 143 | General | analysis | 38 | General |
| multiple stressor | 114 | General | chemical | 38 | Ecotoxicology |
| temperature | 112 | General | climate | 38 | General |
| species | 106 | General | management | 38 | General |
| impact | 104 | General | CO ₂ | 37 | General |
| level | 97 | General | mechanism | 37 | General |
| factor | 90 | General | sediment | 37 | General |
| condition | 88 | General | development | 35 | General |
| ecosystem | 85 | General | habitat | 35 | General |
| experiment | 85 | General | loss | 35 | General |
| stress | 80 | General | soil | 35 | Terrestrial |
| exposure | 72 | General | abundance | 32 | General |
| community | 69 | General | acidification | 32 | Marine |
| combination | 68 | General | diversity | 32 | General |
| growth | 63 | General | hypothesis | 32 | General |
| model | 63 | General | mortality | 32 | General |
| survival | 57 | General | tolerance | 32 | General |
| approach | 55 | General | risk | 31 | Ecotoxicology |
| organism | 55 | General | nitrogen | 30 | General |
| site | 54 | General | year | 30 | General |
| water | 54 | General | competition | 29 | General |
| scale | 52 | General | pesticide | 29 | Ecotoxicology |
| time | 52 | General | risk assessment | 29 | Ecotoxicology |
| interactive effect | 51 | General | fish | 28 | General |
| climate change | 50 | General | relationship | 28 | General |
| increase | 50 | General | driver | 27 | General |
| process | 50 | General | region | 27 | General |
| population | 49 | General | role | 27 | General |
| treatment | 49 | General | synergy | 27 | General |
| salinity | 48 | Marine | eutrophication | 25 | General |
| addition | 46 | General | global change | 25 | General |
| decline | 46 | General | number | 25 | General |
| lake | 46 | Freshwater | precipitation | 25 | Terrestrial |

| river | 25 | Freshwater | metamorphosis | 16 | General |
|------------------------|----|---------------|--------------------------|----|---------------|
| drought | 24 | General | phosphorus | 16 | General |
| reduction | 24 | General | synergistic effect | 16 | General |
| term | 24 | General | synergistic interaction | 16 | General |
| area | 23 | General | toxicant | 16 | Ecotoxicology |
| assessment | 23 | General | use | 16 | General |
| china | 23 | General | water quality | 16 | General |
| consequence | 23 | General | degrees c | 15 | General |
| environmental factor | 23 | General | disease | 15 | General |
| environmental stressor | 23 | General | host | 15 | General |
| hypoxia | 23 | General | individual | 15 | General |
| mixture | 23 | General | local stressor | 15 | General |
| stream | 23 | Freshwater | prediction | 15 | General |
| warming | 23 | General | antagonistic interaction | 14 | General |
| negative effect | 22 | General | elevated CO ₂ | 14 | General |
| research | 22 | General | example | 14 | General |
| review | 22 | General | future | 14 | General |
| action | 21 | General | knowledge | 14 | General |
| anthropogenic stressor | 21 | General | larvae | 14 | General |
| plot | 21 | General | nitrogen deposition | 14 | General |
| toxicity | 21 | Ecotoxicology | oyster | 14 | Marine |
| biodiversity | 20 | General | paper | 14 | General |
| contaminant | 20 | Ecotoxicology | terrestrial ecosystem | 14 | Terrestrial |
| light | 20 | General | water temperature | 14 | General |
| need | 20 | General | aquatic ecosystem | 13 | General |
| coral | 19 | Marine | difference | 13 | General |
| herbivory | 19 | Terrestrial | individual effect | 13 | General |
| land use | 19 | General | order | 13 | General |
| additive effect | 18 | General | reproduction | 13 | General |
| atrazine | 18 | Ecotoxicology | algae | 12 | Marine |
| food | 18 | General | case | 12 | General |
| freshwater ecosystem | 18 | Freshwater | combined effect | 12 | General |
| meta analysis | 18 | General | freshwater | 12 | Freshwater |
| presence | 18 | General | heavy metal | 12 | Ecotoxicology |
| coral reef | 17 | Marine | natural stressor | 12 | General |
| nutrient enrichment | 17 | General | cumulative effect | 11 | General |
| synergism | 17 | General | global change driver | 11 | General |
| variation | 17 | General | magnitude | 11 | General |
| variety | 17 | General | antagonism | 10 | General |
| amphibian | 16 | General | global climate change | 10 | General |
| component | 16 | General | halophyte | 10 | General |
| contrast | 16 | General | water resource | 10 | General |

SM8: Cross-Discipline Comparison

A review of the literature was carried out to investigate how disciplines differ in their study of the ecological impacts of multiple stressors. Our aim was to compare the predictor and response variables, methods and key findings from meta-analyses of multiple-stressor research across disciplines. Below, we briefly summarize multiple-stressor research in each discipline.

1. Freshwater

Freshwater studies of multiple stressors have involved multi-factorial manipulative experiments focused on identifying the nature of net ecological impacts of paired stressors, and underlying causal mechanisms (4). Here, experimental approaches have ranged from *in vitro* microcosms (e.g., 5, 6, 7) to *in situ* mesocosm studies (e.g., 8, 9, 10). Warming combined with either nutrient enrichment or a chemical pollutant are most frequently studied (4).

Field survey-based approaches have also been employed to quantify the cumulative impacts of multiple stressors on freshwater ecosystems (e.g., 11). Here, geo-spatial analysis is increasingly being integrated into studies performed along environmental gradients (e.g., 12, 13, 14). In certain cases, a combined local-regional approach is taken by combining surveys and manipulative experiments (e.g., 11, 15, 16, 17). Other studies have involved multivariate analyses of long-term environmental and biological monitoring data (18), including paleolimnological investigations (19, 20).

In general, empirical evidence suggests that the cumulative ecological impacts of multiple freshwater stressors are most frequently non-additive. Jackson *et al.* (4) quantitatively

synthesized 286 responses across different levels of biological organization and stressor identities to discover that the net impacts of paired stressors were most often less than the sum of their individual effects (*i.e.* antagonistic interactions). Here, net impacts ranged from being less than to near additive, suggesting that freshwater stressors typically dampen rather than amplify the ecological effect of each other. In a meta-analysis of findings from 29 factorial experiments involving freshwater fish, Lange *et al.* (21) found strong evidence of net effects of stressors being both less than additive and dependent on taxonomic identity and life stage. Synergistic responses to stressors were only evident at larger scales of investigation (21), a finding supported by evidence of nitrogen and phosphorus amplifying the direct effect of each other at the whole-ecosystem level (i.e. nutrient co-limitation; 17, 22). The importance of a dominant single stressor to the net ecological impact of several stressors has been demonstrated experimentally in microbial aquatic environments (5, 7). These findings suggest that the most damaging stressor often masks the effects of other less prevalent stressors, causing antagonistic impacts of multiple stressors in freshwaters, in contrast to the prevalence of synergisms reported in the marine literature (23).

2. Marine

The potential for multiple stressors to drive change in marine ecosystems has been widely recognized for over twenty years (24-26). Much of the early research in marine ecosystems focused on how changes in the trophic structure, often attributed to overharvest or disease, contributed to ecosystem-level phase shifts when coupled with physical disturbance (25). These phenomenological studies were followed by efforts to catalogue and map anthropogenic stressors and model the potential for cumulative effects of multiple stressors in the ocean (27, 28). These maps of cumulative effects were based on assumptions of additivity, but the realization that large swaths of the ocean were exposed to two or more

anthropogenic stressors ignited research on potential "interactive effects". Around the same time, a meta-analysis of all full-factorial multiple-stressor experiments in marine ecosystems (focused primarily on individual species) suggested that it was approximately equally likely that the combined effects of multiple stressors are "additive", "antagonistic" or "synergistic" (29), although the probability of synergisms increased with the number of stressors.

Accelerated rates of global change have brought a renewed emphasis to multiple-stressor research in marine ecosystems. The increases in atmospheric carbon dioxide concentrations that cause global warming drive a series of abiotic changes in the ocean, including warming, stratification (which influences nutrient delivery), acidification, and deoxygenation (30, 31). The ubiquity of these co-occurring changes across the marine environment has led to the development of mechanistic, physiological models, such as the *Oxygen- and Capacity-Limited Thermal Tolerance* model (32) and the *Energy Limited Tolerance* model (33), which predict the combined effects of warming, acidification and deoxygenation. Despite the lack of a broadly accepted framework that describes the combined effects of temperature and carbonate chemistry on marine species or ecosystems, empirical data are accumulating that characterize the combined effects of warming and ocean acidification for a broad diversity of species and communities. Although the interactive effects vary among taxa, meta-analyses of full-factorial laboratory and mesocosm experiments suggest that there is a synergism between warming and ocean acidification (34, 35).

In recent years, marine scientists studying global change have established a standard terminology and a framework for designing multiple-stressor studies, to facilitate a broader understanding through synthesis and meta-analysis (36). Synthesis of other aspects of global change, such as ocean acidification, have benefitted from community-established standards for treatment levels and methods (37). However, the vast number of co-occurring stressors have precluded rigid standards for designing multi-stressor global change experiments. In addition, the recognition that interactions across different levels of organization can exacerbate or dampen the effects of multiple stressors highlights the challenges in predicting their combined effects (38).

3. Terrestrial

Unlike the aquatic realm, terrestrial meta-analyses across a range of multiple stressors are uncommon and tend to focus on pairs of multiple climate change and/or land-use change variables (39-43). In the last few decades, several terrestrial review papers and global meta-analyses of full-factorial designs in the field or in the laboratory have provided much needed benchmark data for understanding how plants and soil might respond to global change factors. Particularly, a slew of experiments have tested the combined effects of increased carbon dioxide concentrations, temperature, drought, nitrogen deposition, radiation and heavy metals (40, 44-46). There is also robust understanding of how eutrophication (excessive addition of nitrogen and phosphorus) may be offset or altered by human-induced herbivory. For example, Borer *et al.* (47) reported from their global-scale field experiment (*Nutrient Network*, <u>http://www.nutnet.umn.edu/</u>) that species loss from anthropogenic eutrophication can be ameliorated in grasslands where herbivory increases ground-level light (i.e.

Both models and experiments have been used in terrestrial ecosystem research to understand the impact of multiple drivers and their interactions on ecosystem parameters. One such interaction commonly described through experimental work is that both elevated carbon dioxide and warming typically increase total plant productivity (but not necessarily standing biomass), but in combination they may have additive, synergistic, or antagonistic outcomes (40, 48). Models, on the other hand, show mainly additive combined effects of these two drivers (49), which has led to major discrepancies between empirical and theoretical evidence (44). One way of testing the interacting effects between multiple stressors in terrestrial ecology is the use of congruent time series on animal populations (or substituting space for time), with climate change and land-use change replicated across landscapes (50). Such analyses have found a fairly consistent synergistic effect between baseline temperature conditions and habitat loss on a range of biological populations (43, 50, 51).

Taking a predictive approach to multiple stressors is another major advance in terrestrial ecology. Identifying areas or species at threat and predicting impacts under multiple interacting scenarios allows for more effective conservation planning and possible intervention. Climate change and land-use change are two stressors commonly projected under different scenarios (52), and the results have generally shown how changing land use could reduce or increase future climate change threats for some habitats and species (e.g., 53), or how climate change will mediate the effects of land-cover change (e.g., 54).

4. Ecotoxicology

Ecotoxicology is a discipline that integrates toxicology and ecology to study the effects of toxic chemicals at multiple biological scales. By describing the biological consequences of toxic chemicals, ecotoxicology underpins ecological risk assessment, which is a process that evaluates the probability of adverse ecological effects as a result of exposure to one or more chemical stressor (55, 56). The most frequently studied multiple stressors in ecotoxicology are mixtures of chemicals (57, 58). Chemical stressors, often referred to as toxicants, are described by their chemistry (*e.g.* polycyclic aromatic hydrocarbons, metals), modes of action

(*e.g.* insecticides, antibiotics) or anthropogenic use (*e.g.* personal care products, flame retardants).

Most of the work addressing interactions between chemical and non-chemical stressors has been done in the context of climate change (59-61), although interactions with water scarcity (62), salinization (63, 64) and biotic stressors such as competition, food limitation, pathogens or predators (65, 66) have also been investigated. These studies either disentangle the effects of multiple stressors from field observations (e.g., 67, 68), or evaluate effects of (mostly two) stressors in factorial experiments usually on single species (e.g., 69) or occasionally on communities (e.g., 70).

Non-chemical stressors can impact the ecological effects of chemical stressors via 1) altering the exposure at the receptor or the susceptibility of the receptor (e.g., 71), 2) interacting effects at different receptors (e.g., 55), 3) effects on different species through ecological interactions (e.g., 72) or 4) changing the bioavailability of toxicants (e.g., 73). Systematic reviews on interactions between chemicals and non-chemical stressors when affecting terrestrial and aquatic environments have been performed, but the majority of these studies are limited to the individual level (65, 74). By studying the effects on individuals only, the ultimate ecological consequences of multiple stressors remain unknown (75, 76). Moreover, the individual species used in these studies are primarily model species, which further increases the uncertainty surrounding their ecological relevancy.

The question "How can interactions among different stress factors operating at different levels of biological organization be accounted for in environmental risk assessment?" was the most important question identified during the recent Society of Environmental Toxicology and Chemistry Europe's 'Global Horizon Scanning' workshop (77). The same topic was also identified as an important research direction in other reviews of the ecotoxicology literature (78, 79). Yet, the evidence produced by ecotoxicological research to date, due to its strong bias towards the individual level, with an overwhelming focus on just a few model species, does not help to answer these questions.

References:

1. Van Eck N, Waltman L. Software survey: VOSviewer, a computer program for bibliometric mapping. Scientometrics. 2009;84(2):523-38.

2. Team RC. R: A language and environment for statistical computing. 2013.

3. Warnes GR, Bolker B, Bonebakker L, Gentleman R, Liaw WHA, Lumley T, et al. gplots: Various R programming tools for plotting data. 2015.

 Jackson MC, Loewen CJ, Vinebrooke RD, Chimimba CT. Net effects of multiple stressors in freshwater ecosystems: a meta-analysis. Global Change Biology. 2016;22(1):180-9.

5. Brennan G, Collins S. Growth responses of a green alga to multiple environmental drivers. Nature Climate Change. 2015;5(9):892.

6. Dinh Van K, Janssens L, Debecker S, De Jonge M, Lambret P, Nilsson-Örtman V, et al. Susceptibility to a metal under global warming is shaped by thermal adaptation along a latitudinal gradient. Global Change Biology. 2013;19(9):2625-33.

7. Garnier A, Pennekamp F, Lemoine M, Petchey OL. Temporal scale dependent interactions between multiple environmental disturbances in microcosm ecosystems. Global Change Biology. 2017;23(12):5237-48.

8. Christensen MR, Graham MD, Vinebrooke RD, Findlay DL, Paterson MJ, Turner MA. Multiple anthropogenic stressors cause ecological surprises in boreal lakes. Global Change Biology. 2006;12(12):2316-22.

9. Matthaei CD, Piggott JJ, Townsend CR. Multiple stressors in agricultural streams: interactions among sediment addition, nutrient enrichment and water abstraction. Journal of Applied Ecology. 2010;47(3):639-49.

10. Piggott JJ, Lange K, Townsend CR, Matthaei CD. Multiple stressors in agricultural streams: a mesocosm study of interactions among raised water temperature, sediment addition and nutrient enrichment. PloS One. 2012;7(11):e49873.

 Hering D, Carvalho L, Argillier C, Beklioglu M, Borja A, Cardoso AC, et al.
 Managing aquatic ecosystems and water resources under multiple stress—An introduction to the MARS project. Science of the Total Environment. 2015;503:10-21.

12. Vörösmarty CJ, McIntyre PB, Gessner MO, Dudgeon D, Prusevich A, Green P, et al. Global threats to human water security and river biodiversity. Nature. 2010;467(7315):555.

13. MacDougall MJ, Paterson AM, Winter JG, Jones FC, Knopf LA, Hall RI. Response of periphytic diatom communities to multiple stressors influencing lakes in the Muskoka River Watershed, Ontario, Canada. Freshwater Science. 2017;36(1):77-89.

14. Kath J, Thomson JR, Thompson RM, Kefford BJ, Dyer FJ, Mac Nally R. Interactions among stressors may be weak: Implications for management of freshwater macroinvertebrate communities. Diversity and Distributions. 2018;24(7):939-50.

15. Jackson MC, Jones T, Milligan M, Sheath D, Taylor J, Ellis A, et al. Niche differentiation among invasive crayfish and their impacts on ecosystem structure and functioning. Freshwater Biology. 2014;59(6):1123-35.

16. Townsend CR, Uhlmann SS, Matthaei CD. Individual and combined responses of stream ecosystems to multiple stressors. Journal of Applied Ecology. 2008;45(6):1810-9.

 Vinebrooke RD, MacLennan MM, Bartrons M, Zettel JP. Missing effects of anthropogenic nutrient deposition on sentinel alpine ecosystems. Global Change Biology. 2014;20(7):2173-82.

18. Palmer ME, Yan ND. Decadal-scale regional changes in C anadian freshwater zooplankton: the likely consequence of complex interactions among multiple anthropogenic stressors. Freshwater Biology. 2013;58(7):1366-78.

19. Hecky R, Mugidde R, Ramlal P, Talbot M, Kling G. Multiple stressors cause rapid ecosystem change in Lake Victoria. Freshwater Biology. 2010;55:19-42.

20. Röhland KM, Paterson AM, Hargan K, Jenkin A, Clark BJ, Smol JP. Reorganization of algal communities in the Lake of the Woods (Ontario, Canada) in response to turn-of-thecentury damming and recent warming. Limnology and Oceanography. 2010;55(6):2433-51. 21. Lange K, Bruder A, Matthaei CD, Brodersen J, Paterson RA. Multiple-stressor effects on freshwater fish: Importance of taxonomy and life stage. Fish and Fisheries. 2018.

22. Elser JJ, Bracken ME, Cleland EE, Gruner DS, Harpole WS, Hillebrand H, et al. Global analysis of nitrogen and phosphorus limitation of primary producers in freshwater, marine and terrestrial ecosystems. Ecology Letters. 2007;10(12):1135-42.

23. Côté IM, Darling ES, Brown CJ. Interactions among ecosystem stressors and their importance in conservation. Proceedings of the Royal Society B. 2016;283(1824):20152592.

24. Breitburg DL, Baxter JW, Hatfield CA, Howarth RW, Jones CG, Lovett GM, et al. Understanding effects of multiple stressors: ideas and challenges. Successes, Limitations, and Frontiers in Ecosystem Science: Springer; 1998. p. 416-31.

25. Hughes T, Connell J. Multiple stressors on coral reefs: A long-term perspective. Limnology and Oceanography. 1999;44(3):932-40.

26. Micheli F. Eutrophication, fisheries, and consumer-resource dynamics in marine pelagic ecosystems. Science. 1999;285(5432):1396-8.

27. Halpern BS, Walbridge S, Selkoe KA, Kappel CV, Micheli F, D'agrosa C, et al. A global map of human impact on marine ecosystems. Science. 2008;319(5865):948-52.

28. Ban N, Alder J. How wild is the ocean? Assessing the intensity of anthropogenic marine activities in British Columbia, Canada. Aquatic Conservation: Marine and Freshwater Ecosystems. 2008;18(1):55-85.

29. Crain CM, Kroeker K, Halpern BS. Interactive and cumulative effects of multiple human stressors in marine systems. Ecology Letters. 2008;11(12):1304-15.

 Boyd PW, Hutchins DA. Understanding the responses of ocean biota to a complex matrix of cumulative anthropogenic change. Marine Ecology Progress Series. 2012;470:125-35.

31. Harley CD, Randall Hughes A, Hultgren KM, Miner BG, Sorte CJ, Thornber CS, et
al. The impacts of climate change in coastal marine systems. Ecology Letters. 2006;9(2):22841.

32. Pörtner H-O. Oxygen-and capacity-limitation of thermal tolerance: a matrix for integrating climate-related stressor effects in marine ecosystems. Journal of Experimental Biology. 2010;213(6):881-93.

33. Sokolova IM. Energy-limited tolerance to stress as a conceptual framework to integrate the effects of multiple stressors. Integrative and Comparative Biology.
2013;53(4):597-608.

34. Przesławski R, Byrne M, Mellin C. A review and meta-analysis of the effects of multiple abiotic stressors on marine embryos and larvae. Global Change Biology.
2015;21(6):2122-40.

35. Kroeker KJ, Micheli F, Gambi MC. Ocean acidification causes ecosystem shifts via altered competitive interactions. Nature Climate Change. 2013;3(2):156.

36. Boyd PW, Collins S, Dupont S, Fabricius K, Gattuso JP, Havenhand J, et al. Experimental strategies to assess the biological ramifications of multiple drivers of global ocean change—a review. Global Change Biology. 2018;24(6):2239-61.

37. Riebesell U, Fabry VJ, Hansson L, Gattuso J-P. Guide to best practices for ocean acidification research and data reporting: Office for Official Publications of the European Communities; 2011.

38. Kroeker KJ, Kordas RL, Harley CD. Embracing interactions in ocean acidification research: confronting multiple stressor scenarios and context dependence. Biology Letters. 2017;13(3):20160802.

39. Bancroft BA, Baker NJ, Blaustein AR. A meta-analysis of the effects of ultraviolet B radiation and its synergistic interactions with pH, contaminants, and disease on amphibian survival. Conservation Biology. 2008;22(4):987-96.

40. Dieleman WI, Vicca S, Dijkstra FA, Hagedorn F, Hovenden MJ, Larsen KS, et al. Simple additive effects are rare: a quantitative review of plant biomass and soil process responses to combined manipulations of CO₂ and temperature. Global Change Biology. 2012;18(9):2681-93. 41. Wu Z, Dijkstra P, Koch GW, Peñuelas J, Hungate BA. Responses of terrestrial ecosystems to temperature and precipitation change: a meta-analysis of experimental manipulation. Global Change Biology. 2011;17(2):927-42.

42. Rosenblatt AE, Schmitz OJ. Interactive effects of multiple climate change variables on trophic interactions: a meta-analysis. Climate Change Responses. 2014;1(1):8.

43. Mantyka-Pringle CS, Martin TG, Rhodes JR. Interactions between climate and habitat loss effects on biodiversity: a systematic review and meta-analysis. Global Change Biology. 2012;18(4):1239-52.

44. Leuzinger S, Luo Y, Beier C, Dieleman W, Vicca S, Körner C. Do global change experiments overestimate impacts on terrestrial ecosystems? Trends in Ecology & Evolution. 2011;26(5):236-41.

45. Yue K, Fornara DA, Yang W, Peng Y, Li Z, Wu F, et al. Effects of three global change drivers on terrestrial C: N: P stoichiometry: a global synthesis. Global Change Biology. 2017;23(6):2450-63.

46. Vanhoudt N, Vandenhove H, Real A, Bradshaw C, Stark K. A review of multiple stressor studies that include ionising radiation. Environmental Pollution. 2012;168:177-92.

47. Borer ET, Seabloom EW, Gruner DS, Harpole WS, Hillebrand H, Lind EM, et al.
Herbivores and nutrients control grassland plant diversity via light limitation. Nature.
2014;508(7497):517.

48. McCarthy HR, Oren R, Finzi AC, Ellsworth DS, Kim HS, Johnsen KH, et al. Temporal dynamics and spatial variability in the enhancement of canopy leaf area under elevated atmospheric CO₂. Global Change Biology. 2007;13(12):2479-97.

49. Luo Y, Gerten D, Le Maire G, Parton WJ, Weng E, Zhou X, et al. Modeled interactive effects of precipitation, temperature, and [CO₂] on ecosystem carbon and water dynamics in different climatic zones. Global Change Biology. 2008;14(9):1986-99.

50. Northrup JM, Rivers JW, Yang Z, Betts MG. Synergistic effects of climate and landuse change influence broad-scale avian population declines. Global Change Biology. 2019. 51. Guo F, Lenoir J, Bonebrake TC. Land-use change interacts with climate to determine elevational species redistribution. Nature Communications. 2018;9(1):1315.

52. Oliver TH, Marshall HH, Morecroft MD, Brereton T, Prudhomme C, Huntingford C. Interacting effects of climate change and habitat fragmentation on drought-sensitive butterflies. Nature Climate Change. 2015;5(10):941.

53. Mair L, Jönsson M, Räty M, Bärring L, Strandberg G, Lämås T, et al. Land use changes could modify future negative effects of climate change on old-growth forest indicator species. Diversity and Distributions. 2018;24(10):1416-25.

54. Mantyka-Pringle CS, Visconti P, Di Marco M, Martin TG, Rondinini C, Rhodes JR. Climate change modifies risk of global biodiversity loss due to land-cover change. Biological Conservation. 2015;187:103-11.

55. Ankley GT, Bennett RS, Erickson RJ, Hoff DJ, Hornung MW, Johnson RD, et al. Adverse outcome pathways: a conceptual framework to support ecotoxicology research and risk assessment. Environmental Toxicology and Chemistry: An International Journal. 2010;29(3):730-41.

 Jain R, Urban L, Balbach H, Webb MD. Contemporary issues in environmental assessment. Handbook of Environmental Engineering Assessment Elsevier, Boston.
 2012:361-447.

57. Godoy AA, Kummrow F. What do we know about the ecotoxicology of pharmaceutical and personal care product mixtures? A critical review. Critical Reviews in Environmental Science and Technology. 2017;47(16):1453-96.

58. Posthuma L, van Gils J, Zijp MC, van de Meent D, de Zwart D. Species Sensitivity Distributions for use in Environmental Protection, Assessment and Management of Aquatic Ecosystems for 12,386 Chemicals. Environmental Toxicology and Chemistry. 2019.

59. Moe SJ, De Schamphelaere K, Clements WH, Sorensen MT, Van den Brink PJ, Liess M. Combined and interactive effects of global climate change and toxicants on populations and communities. Environmental Toxicology and Chemistry. 2013;32(1):49-61.

60. Hooper MJ, Ankley GT, Cristol DA, Maryoung LA, Noyes PD, Pinkerton KE. Interactions between chemical and climate stressors: A role for mechanistic toxicology in assessing climate change risks. Environmental Toxicology and Chemistry. 2013;32(1):32-48.

61. Noyes PD, McElwee MK, Miller HD, Clark BW, Van Tiem LA, Walcott KC, et al.The toxicology of climate change: environmental contaminants in a warming world.Environment International. 2009;35(6):971-86.

62. Arenas-Sánchez A, Rico A, Vighi M. Effects of water scarcity and chemical pollution in aquatic ecosystems: state of the art. Science of the Total Environment. 2016;572:390-403.

63. Schäfer RB, Bundschuh M, Rouch DA, Szöcs E, Peter C, Pettigrove V, et al. Effects of pesticide toxicity, salinity and other environmental variables on selected ecosystem functions in streams and the relevance for ecosystem services. Science of the Total Environment. 2012;415:69-78.

64. Szöcs E, Kefford BJ, Schäfer RB. Is there an interaction of the effects of salinity and pesticides on the community structure of macroinvertebrates? Science of the Total Environment. 2012;437:121-6.

65. Holmstrup M, Bindesbøl A-M, Oostingh GJ, Duschl A, Scheil V, Köhler H-R, et al. Interactions between effects of environmental chemicals and natural stressors: a review. Science of the Total Environment. 2010;408(18):3746-62.

66. Liess M, Foit K, Knillmann S, Schäfer RB, Liess H-D. Predicting the synergy of multiple stress effects. Scientific Reports. 2016;6:32965.

67. Rico A, Van den Brink PJ, Leitner P, Graf W, Focks A. Relative influence of chemical and non-chemical stressors on invertebrate communities: a case study in the Danube River. Science of the Total Environment. 2016;571:1370-82.

68. Posthuma L, Dyer SD, de Zwart D, Kapo K, Holmes CM, Burton Jr GA. Ecoepidemiology of aquatic ecosystems: Separating chemicals from multiple stressors. Science of the Total Environment. 2016;573:1303-19. 69. Zhang C, Jansen M, De Meester L, Stoks R. Thermal evolution offsets the elevated toxicity of a contaminant under warming: A resurrection study in Daphnia magna. Evolutionary Applications. 2018;11(8):1425-36.

70. Buck JC, Scheessele EA, Relyea RA, Blaustein AR. The effects of multiple stressors on wetland communities: pesticides, pathogens and competing amphibians. Freshwater Biology. 2012;57(1):61-73.

71. Bednarska AJ, Choczyński M, Laskowski R, Walczak M. Combined effects of chlorpyriphos, copper and temperature on acetylcholinesterase activity and toxicokinetics of the chemicals in the earthworm *Eisenia fetida*. Environmental Pollution. 2017;220:567-76.

72. Traas TP, Janse JH, Van den Brink PJ, Brock TC, Aldenberg T. A freshwater food web model for the combined effects of nutrients and insecticide stress and subsequent recovery. Environmental Toxicology and Chemistry: An International Journal. 2004;23(2):521-9.

73. Løkke H, Ragas AM, Holmstrup M. Tools and perspectives for assessing chemical mixtures and multiple stressors. Toxicology. 2013;313(2-3):73-82.

74. Heugens EH, Hendriks AJ, Dekker T, Straalen NMv, Admiraal W. A review of the effects of multiple stressors on aquatic organisms and analysis of uncertainty factors for use in risk assessment. Critical Reviews in Toxicology. 2001;31(3):247-84.

75. Schäfer RB, Piggott JJ. Advancing understanding and prediction in multiple stressor research through a mechanistic basis for null models. Global Change Biology.
2018;24(5):1817-26.

76. De Laender F. Community-and ecosystem-level effects of multiple environmental change drivers: beyond null model testing. Global Change Biology. 2018.

77. Van den Brink PJ, Boxall AB, Maltby L, Brooks BW, Rudd MA, Backhaus T, et al.
Toward sustainable environmental quality: Priority research questions for Europe.
Environmental Toxicology and Chemistry. 2018;37(9):2281-95.

78. Nilsen E, Smalling KL, Ahrens L, Gros M, Miglioranza KS, Picó Y, et al. Critical review: Grand challenges in assessing the adverse effects of contaminants of emerging concern on aquatic food webs. Environmental Toxicology and Chemistry. 2019;38(1):46-60.

79. Van den Brink PJ, Bracewell SA, Bush A, Chariton A, Choung CB, Compson ZG, et al. Towards a general framework for the assessment of interactive effects of multiple stressors on aquatic ecosystems: Results from the Making Aquatic Ecosystems Great Again (MAEGA) workshop. Science of The Total Environment. 2019.