

Supplementary Information

What is “Environmentally Relevant”? A Framework to Advance Research on the Environmental Fate and Effects of Engineered Nanomaterials

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11 Pages, 5 Tables

Details of Literature Search

A literature search was performed using Web of Science (WoS) to generate a group of studies for use in the illustrative meta-analysis presented and discussed in the main text. The WoS search was performed on December 18th, 2020 using the search parameters presented in Table S1, which generated $n = 437$ individual publications. Based on a cursory review of the initial search results it became apparent that some of the publications that were returned, while meeting the search criteria, were not relevant to the context of the meta-analysis (i.e., the fate, transport, and effects of CuNPs in freshwater environments). Thus, the results were further refined using the “WoS Categories” field to select research fields relevant to the intent of the illustrative meta-analysis (Table S2), generating a reduced list of publications ($n = 99$) that served as the basis for the meta-analysis (detailed below).

Table S1. Parameters used in Web of Science literature search.

| Parameter | Search Terms |
|------------------------|--|
| Title | [(“copper” AND “nano*”) OR (“CuNP*” OR “CuO NP*”)] AND |
| Topic | (“fate” OR “tox*” OR “transport”) AND |
| Topic | (“aquatic” OR “water”) AND |
| Type | Article |
| Language | English |
| Publication Date Range | 2010 – 2020 |

Table S2. Selected research categories and number of publications per category ($n = 99$).

| WoS Categories | Count |
|---|-------|
| Chemistry, Analytical; Environmental Sciences | 2 |
| Chemistry, Multidisciplinary; Environmental Sciences; Nanoscience & Nanotechnology | 6 |
| Ecology; Environmental Sciences | 1 |
| Ecology; Environmental Sciences; Toxicology | 1 |
| Environmental Sciences | 61 |
| Environmental Sciences; Nanoscience & Nanotechnology | 1 |
| Environmental Sciences; Toxicology | 19 |
| Nanoscience & Nanotechnology; Toxicology | 5 |
| Toxicology | 3 |

Meta-Analysis and Placement of Individual Studies

As the intent of the meta-analysis was to prepare an illustrative example of how our conceptual framework could be applied, as opposed to an exhaustive review, the reduced list of publications generated by the WoS search ($n = 99$) was further refined in scope through the following steps. First, the title and abstract of each paper was reviewed to confirm it fit the context of the meta-analysis (i.e., the fate, transport, and effects of CuNPs in freshwater environments), which reduced the list to $n = 55$ publications (Table S4). Then, a representative proportion (targeting $\approx 50\%$) were randomly selected using a random number generator that accounted for the distribution in publication years of the list presented in Table S3. When necessary, the number of publications that were carried forward into the meta-analysis for a given year was rounded up. For example, of the 55 publications presented in Table S3, 3 were published in 2012 (representing $\approx 5\%$ of the total; $n = 55$). Of this, 2 were randomly selected and used in the meta-analysis (representing $\approx 7\%$ of total; $n = 29$). The list of publications used in the meta-analysis, along with the values assigned to each of the three pillars (per the rubric presented in the main text), are presented in Table S5.

Table S3. Distribution and weighting of papers used as inputs to the meta-analysis.

| Year | Total Count | Percent of Total | Weighted Number Included | Percent of Total |
|-------|-------------|------------------|--------------------------|------------------|
| 2010 | 0 | 0% | 0 | 0% |
| 2011 | 1 | 2% | 1 | 3% |
| 2012 | 3 | 5% | 2 | 7% |
| 2013 | 1 | 2% | 1 | 3% |
| 2014 | 8 | 15% | 4 | 14% |
| 2015 | 10 | 18% | 5 | 17% |
| 2016 | 6 | 11% | 3 | 10% |
| 2017 | 6 | 11% | 3 | 10% |
| 2018 | 6 | 11% | 3 | 10% |
| 2019 | 8 | 15% | 4 | 14% |
| 2020 | 6 | 11% | 3 | 10% |
| Total | 55 | 100% | 29 | 100% |

Table S4. Initial list of publications used in meta-analysis ($n = 55$).

| Authors | Title | Journal | Year | Volume | Issue | DOI |
|--|---|---|------|--------|-------|-----------------------------------|
| Shi, JY; Abid, AD; Kennedy, IM; Hristova, KR; Silk, WK | To Duckweeds (<i>Landoltia Punctata</i>), Nanoparticulate Copper Oxide is More Inhibitory than the Soluble Copper in the Bulk Solution | Environmental Pollution | 2011 | 159 | 5 | 10.1016/j.envpol.2011.01.028 |
| Manusadzianas, L; Caillet, C; Fachetti, L; Gyllyte, B; Grigutyte, R; Jurkoniene, S; Karitonas, R; Sadauskas, K; Thomas, F; Vitkus, R; Ferard, JF | Toxicity of Copper Oxide Nanoparticle Suspensions to Aquatic Biota | Environmental Toxicology and Chemistry | 2012 | 31 | 1 | 10.1002/etc.715 |
| Perreault, F; Oukarroum, A; Melegari, SP; Matias, WG; Popovic, R | Polymer Coating of Copper Oxide Nanoparticles increases Nanoparticles Uptake and Toxicity in the Green Alga <i>Chlamydomonas Reinhardtii</i> | Chemosphere | 2012 | 87 | 11 | 10.1016/j.chemosphere.2012.02.046 |
| Pradhan, A; Seena, S; Pascoal, C; Cassio, F | Copper Oxide Nanoparticles Can Induce Toxicity to the Freshwater Shredder <i>Allogamus Ligonifer</i> | Chemosphere | 2012 | 89 | 9 | 10.1016/j.chemosphere.2012.06.001 |
| Pang, CF; Selck, H; Banta, GT; Misra, SK; Berhanu, D; Dybowska, A; Valsami-Jones, E; Forbes, VE | Bioaccumulation, toxicokinetics, and Effects of Copper from Sediment Spiked with Aqueous Cu, Nano-CuO, or Micro-CuO in the Deposit-Feeding Snail, <i>Potamopyrgus Antipodarum</i> | Environmental Toxicology and Chemistry | 2013 | 30 | 7 | 10.1002/etc.2216 |
| Rai, M; Ingle, A; Gupta, I; Gaikwad, S; Gade, A; Rubilar, O; Duran, N | Cyto-, Geno-, and Ecotoxicity of Copper Nanoparticles | Nanotoxicology: Materials, Methodologies, and Assessments | 2014 | | | 10.1007/978-1-4614-8993-1_15 |
| Perreault, F; Samadani, M; Dewez, D | Effect of Soluble Copper Released from Copper Oxide Nanoparticles Solubilisation on Growth and Photosynthetic Processes of <i>Lemna Gibba L</i> | Nanotoxicology | 2014 | 8 | 4 | 10.3109/17435390.2013.789936 |
| Han, X; Geller, B; Moniz, K; Das, P; Chippindale, AK; Walker, VK | Monitoring the Developmental Impact of Copper and Silver Nanoparticle Exposure in <i>Drosophila</i> and their Microbiomes | Science of the total Environment | 2014 | 487 | | 10.1016/j.scitotenv.2013.12.129 |
| Ma, R; Stegemeier, J; Levard, C; Dale, JG; Noack, CW; Yang, T; Brown, GE; Lowry, GV | Sulfidation of Copper Oxide Nanoparticles and Properties of Resulting Copper Sulfide | Environmental Science-Nano | 2014 | 1 | 4 | 10.1039/c4en00018h |
| Rossetto, ALDF; Vicentini, DS; Costa, CH; Melegari, SP; Matias, WG | Synthesis, Characterization and toxicological Evaluation of a Core-Shell Copper Oxide/Polyaniline Nanocomposite | Chemosphere | 2014 | 108 | | 10.1016/j.chemosphere.2014.03.038 |

Table S4. Initial list of publications used in meta-analysis ($n = 55$).

| Authors | Title | Journal | Year | Volume | Issue | DOI |
|--|--|--|------|--------|-------|-----------------------------------|
| Ramkov, T; Selck, H; Banta, G; Misra, SK; Berhanu, D; Valsami-Jones, E; forbes, VE | Bioaccumulation and Effects of Different-Shaped Copper Oxide Nanoparticles in the Deposit-Feeding Snail <i>Potamopyrgus Antipodarum</i> | Environmental Toxicology and Chemistry | 2014 | 33 | 9 | 10.1002/etc.2639 |
| Majedi, SM; Kelly, BC; Lee, HK | Toward a Robust Analytical Method for Separating Trace Levels of Nano-Materials in Natural Waters: Cloud Point Extraction of Nano-Copper(II) Oxide | Environmental Science and Pollution Research | 2014 | 21 | 20 | 10.1007/s11356-013-2381-7 |
| Sankar, R; Prasath, BB; Nandakumar, R; Santhanam, P; Shivashangari, KS; Ravikumar, V | Growth inhibition of Bloom forming Cyanobacterium <i>Microcystis Aeruginosa</i> by Green Route Fabricated Copper Oxide Nanoparticles | Environmental Science and Pollution Research | 2014 | 21 | 24 | 10.1007/s11356-014-3362-1 |
| Pradhan, A; Seena, S; Schlosser, D; Gerth, K; Helm, S; Dobritzsch, M; Krauss, GJ; Dobritzsch, D; Pascoal, C; Cassio, F | Fungi from Metal-Polluted Streams May Have High Ability to Cope with the Oxidative Stress induced by Copper Oxide Nanoparticles | Environmental Toxicology and Chemistry | 2015 | 34 | 4 | 10.1002/etc.2879 |
| Reyes, VC; Opot, SO; Mahendra, S | Planktonic and Biofilm-Grown Nitrogen-Cycling Bacteria Exhibit Different Susceptibilities to Copper Nanoparticles | Environmental Toxicology and Chemistry | 2015 | 34 | 4 | 10.1002/etc.2867 |
| Son, J; Vavra, J; Li, YS; Seymour, M; forbes, V | Interactions Between Suspension Characteristics and Physicochemical Properties of Silver and Copper Oxide Nanoparticles: A Case Study for Optimizing Nanoparticle Stock Suspensions Using A Central Composite Design | Chemosphere | 2015 | 124 | | 10.1016/j.chemosphere.2014.12.005 |
| Regier, N; Cosio, C; von Moos, N; Slaveykova, VI | Effects of Copper-Oxide Nanoparticles, Dissolved Copper and Ultraviolet Radiation on Copper Bioaccumulation, Photosynthesis and Oxidative Stress in the Aquatic Macrophyte <i>Elodea Nuttallii</i> | Chemosphere | 2015 | 128 | | 10.1016/j.chemosphere.2014.12.078 |
| Song, L; Vijver, MG; Peijnenburg, WJGM | Comparative Toxicity of Copper Nanoparticles Across Three <i>Lemnaceae</i> Species | Science of the total Environment | 2015 | 518 | | 10.1016/j.scitotenv.2015.02.079 |
| Son, J; Vavra, J; forbes, VE | Effects of Water Quality Parameters on Agglomeration and Dissolution of Copper Oxide Nanoparticles (CuO-NPs) Using A Central Composite Circumscribed Design | Science of the total Environment | 2015 | 521 | | 10.1016/j.scitotenv.2015.03.093 |

Table S4. Initial list of publications used in meta-analysis ($n = 55$).

| Authors | Title | Journal | Year | Volume | Issue | DOI |
|---|---|--|------|--------|-------|-----------------------------------|
| Thit, A; Banta, GT; Selck, H | Bioaccumulation, Subcellular Distribution and Toxicity of Sediment-Associated Copper in the Ragworm <i>Nereis Diversicolor</i> : The Relative Importance of Aqueous Copper, Copper Oxide Nanoparticles and Microparticles | Environmental Pollution | 2015 | 202 | | 10.1016/j.envpol.2015.02.025 |
| Nations, S; Long, M; Wages, M; Maul, JD; theodorakis, CW; Cobb, GP | Subchronic and Chronic Developmental Effects of Copper Oxide (CuO) Nanoparticles on <i>Xenopus Laevis</i> | Chemosphere | 2015 | 135 | | 10.1016/j.chemosphere.2015.03.078 |
| Song, L; Vijver, MG; Peijnenburg, WJGM; Galloway, TS; Tyler, CR | A Comparative Analysis on the in Vivo Toxicity of Copper Nanoparticles in Three Species of Freshwater Fish | Chemosphere | 2015 | 139 | | 10.1016/j.chemosphere.2015.06.021 |
| Shang, EX; Li, Y; Niu, JF; Guo, HY; Zhou, YJ; Liu, H; Zhang, XQ | Effect of Aqueous Media on the Copper-Ion-Mediated Phototoxicity of CuO Nanoparticles toward Green Fluorescent Protein-Expressing <i>Escherichia Coli</i> | Ecotoxicology and Environmental Safety | 2015 | 122 | | 10.1016/j.ecoenv.2015.08.002 |
| Muller, E; Behra, R; Sigg, L | Toxicity of Engineered Copper (Cu-0) Nanoparticles to the Green Alga <i>Chlamydomonas Reinhardtii</i> | Environmental Chemistry | 2016 | 13 | 3 | 10.1071/EN15130 |
| Ostaszewska, T; Chojnacki, M; Kamaszewski, M; Sawosz-Chwalibog, E | Histopathological Effects of Silver and Copper Nanoparticles on the Epidermis, Gills, and Liver of Siberian Sturgeon | Environmental Science and Pollution Research | 2016 | 23 | 2 | 10.1007/s11356-015-5391-9 |
| Gonzalez-Estrella, J; Gallagher, S; Sierra-Alvarez, R; Field, JA | Iron Sulfide Attenuates the Methanogenic Toxicity of Elemental Copper and Zinc Oxide Nanoparticles and their Soluble Metal Ion Analogs | Science of the total Environment | 2016 | 548 | | 10.1016/j.scitotenv.2016.01.006 |
| Wang, Z; Fang, H; Wang, S | Benzoic Acid interactions Affect Aquatic Properties and Toxicity of Copper Oxide Nanoparticles | Bulletin of Environmental Contamination and Toxicology | 2016 | 97 | 2 | 10.1007/s00128-016-1804-9 |
| Xiao, YL; Peijnenburg, WJGM; Chen, GC; Vijver, MG | Toxicity of Copper Nanoparticles to <i>Daphnia Magna</i> Under Different Exposure Conditions | Science of the total Environment | 2016 | 563 | | 10.1016/j.scitotenv.2016.04.104 |
| Mansouri, B; Maleki, A; Johari, SA; Shahmoradi, B; Mohammadi, E; Shahsavari, S; Davari, B | Copper Bioaccumulation and Depuration in Common Carp (<i>Cyprinus Carpio</i>) Following Co-Exposure to Tio2 and CuO Nanoparticles | Archives of Environmental Contamination and Toxicology | 2016 | 71 | 4 | 10.1007/s00244-016-0313-5 |
| Thit, A; Huggins, K; Selck, H; Baun, | Acute Toxicity of Copper Oxide Nanoparticles to <i>Daphnia Magna</i> Under | toxicological and | 2017 | 99 | 4 | 10.1080/02772248.2016.1249368 |

Table S4. Initial list of publications used in meta-analysis ($n = 55$).

| Authors | Title | Journal | Year | Volume | Issue | DOI |
|---|--|--|------|--------|-------|---------------------------------|
| A | Different Test Conditions | Environmental Chemistry | | | | |
| Black, MN; Henry, EF; Adams, OA; Bennett, JCF; MacCormack, TJ | Environmentally Relevant Concentrations of Amine-Functionalized Copper Nanoparticles Exhibit Different Mechanisms of Bioactivity in <i>Fundulus Heteroclitus</i> in Fresh and Brackish Water | Nanotoxicology | 2017 | 11 | 8 | 10.1080/17435390.2017.1395097 |
| Karimi, R; Norastehnia, A; Abbaspour, H; Saeidisar, S; Naeemi, AS | Toxicity Assessment of <i>Anabaena Sp.</i> Following Exposure to Copper Oxide Nanoparticles and Sodium Chloride | Applied Ecology and Environmental Research | 2017 | 15 | 4 | 10.15666/aeer/1504_20452059 |
| Liu, YX; Yan, ZH; Xia, J; Wang, K; Ling, XC; Yan, B | Potential Toxicity in Crucian Carp Following Exposure to Metallic Nanoparticles of Copper, Chromium, and their Mixtures: A Comparative Study | Polish Journal of Environmental Studies | 2017 | 26 | 5 | 10.15244/pjoes/69251 |
| Moustakas, M; Malea, P; Haritonidou, K; Sperdouli, I | Copper Bioaccumulation, Photosystem II Functioning, and Oxidative Stress in the Seagrass <i>Cymodocea Nodosa</i> Exposed to Copper Oxide Nanoparticles | Environmental Science and Pollution Research | 2017 | 24 | 19 | 10.1007/s11356-017-9174-3 |
| Thit, A; Skjolding, LM; Selck, H; Sturve, J | Effects of Copper Oxide Nanoparticles and Copper Ions to Zebrafish (<i>Danio rerio</i>) Cells, Embryos and Fry | Toxicology in Vitro | 2017 | 45 | | 10.1016/j.tiv.2017.08.010 |
| Xiao, YL; Peijnenburg, WJGM; Chen, GC; Vijver, MG | Impact of Water Chemistry on the Particle-Specific Toxicity of Copper Nanoparticles to <i>Daphnia Magna</i> | Science of the total Environment | 2018 | 610 | | 10.1016/j.scitotenv.2017.08.188 |
| Vicario-Pares, U; Lacave, JM; Reip, P; Cajaraville, MP; orbea, A | Cellular and Molecular Responses of Adult Zebrafish After Exposure to CuO Nanoparticles or Ionic Copper | Ecotoxicology | 2018 | 27 | 1 | 10.1007/s10646-017-1873-5 |
| Xiao, YL; Vijver, MG; Peijnenburg, WJGM | Impact of Water Chemistry on the Behavior and Fate of Copper Nanoparticles | Environmental Pollution | 2018 | 234 | | 10.1016/j.envpol.2017.12.015 |
| Shahzad, K; Khan, MN; Jabeen, F; Kosour, N; Chaudhry, AS; Sohail, M | Evaluating Toxicity of Copper(II) Oxide Nanoparticles (CuO-NPs) Through Waterborne Exposure to Tilapia (<i>Oreochromis Mossambicus</i>) by Tissue Accumulation, Oxidative Stress, Histopathology, and Genotoxicity | Environmental Science and Pollution Research | 2018 | 25 | 16 | 10.1007/s11356-018-1813-9 |
| Braz-Mota, S; Campos, DF; MacCormack, TJ; Duarte, RM; Val, AL; Almeida-Val, VMF | Mechanisms of Toxic Action of Copper and Copper Nanoparticles in Two Amazon Fish Species: Dwarf Cichlid (<i>Apistogramma Agassizii</i>) and Cardinal Tetra (<i>Paracheirodon Axeirodi</i>) | Science of the total Environment | 2018 | 630 | | 10.1016/j.scitotenv.2018.02.216 |

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| Authors | Title | Journal | Year | Volume | Issue | DOI |
|---|--|--|------|--------|-------|-----------------------------------|
| Mansano, AS; Souza, JP; Cancino-Bernardi, J; Venturini, FP; Marangoni, VS; Zucolotto, V | Toxicity of Copper Oxide Nanoparticles to Neotropical Species <i>Ceriodaphnia Silvestrii</i> and <i>Hyphessobrycon Eques</i> | Environmental Pollution | 2018 | 243 | | 10.1016/j.envpol.2018.09.020 |
| Miao, LZ; Wang, PF; Hou, J; Yao, Y; Liu, ZL; Liu, SQ | Low Concentrations of Copper Oxide Nanoparticles Alter Microbial Community Structure and Function of Sediment Biofilms | Science of the total Environment | 2019 | 653 | | 10.1016/j.scitotenv.2018.10.354 |
| Barreto, DM; tonietto, AE; Amaral, CDB; Pulgrossi, RC; Polpo, A; Nobrega, JA; Lombardi, AT | Physiological Responses of <i>Chlorella Sorokiniana</i> to Copper Nanoparticles | Environmental Toxicology and Chemistry | 2019 | 38 | 2 | 10.1002/etc.4330 |
| Yang, L; Wang, WX | Comparative Contributions of Copper Nanoparticles and Ions to Copper Bioaccumulation and Toxicity in Barnacle Larvae | Environmental Pollution | 2019 | 249 | | 10.1016/j.envpol.2019.02.103 |
| Arenas-Lago, D; Monikh, FA; Vijver, MG; Peijnenburg, WJGM | Dissolution and Aggregation Kinetics of Zero Valent Copper Nanoparticles in (Simulated) Natural Surface Waters: Simultaneous Effects of Ph, NOM and Ionic Strength | Chemosphere | 2019 | 226 | | 10.1016/j.chemosphere.2019.03.190 |
| Ogunsuyi, OI; Fadoju, OM; Akanni, OO; Alabi, OA; Alimba, CG; Cambier, S; Eswara, S; Gutleb, AC; Adaramoye, OA; Bakare, AA | Genetic and Systemic Toxicity induced by Silver and Copper Oxide Nanoparticles, and their Mixture in <i>Clarias Gariepinus</i> (Burchell, 1822) | Environmental Science and Pollution Research | 2019 | 26 | 26 | 10.1007/s11356-019-05956-6 |
| Parsai, T; Kumar, A | Understanding Effect of Solution Chemistry on Heteroaggregation of Zinc Oxide and Copper Oxide Nanoparticles | Chemosphere | 2019 | 235 | | 10.1016/j.chemosphere.2019.06.171 |
| Kansara, K; Paruthi, A; Misra, SK; Karakoti, AS; Kumar, A | Montmorillonite Clay and Humic Acid Modulate the Behavior of Copper Oxide Nanoparticles in Aqueous Environment and Induces Developmental Defects in Zebrafish Embryo | Environmental Pollution | 2019 | 255 | | 10.1016/j.envpol.2019.113313 |
| Seena, S; Kumar, S | Short-Term Exposure to Low Concentrations of Copper Oxide Nanoparticles Can Negatively Impact the Ecological Performance of a Cosmopolitan Freshwater Fungus | Environmental Science-Processes & Impacts | 2019 | 21 | 12 | 10.1039/c9em00361d |
| Tesser, ME; de Paula, AA; Risso, WE; Monteiro, RA; Pereira, ADS; Fraceto, LF; Martinez, CBD | Sublethal Effects of Waterborne Copper and Copper Nanoparticles on the Freshwater Neotropical Teleost <i>Prochilodus Lineatus</i> : A Comparative Approach | Science of the total Environment | 2020 | 704 | | 10.1016/j.scitotenv.2019.135330 |
| Boyle, D; Clark, NJ; Handy, RD | Toxicities of Copper Oxide Nanomaterial and Copper Sulphate in Early | Ecotoxicology and | 2020 | 190 | | 10.1016/j.ecoenv.2019.109985 |

Table S4. Initial list of publications used in meta-analysis ($n = 55$).

| Authors | Title | Journal | Year | Volume | Issue | DOI |
|---|--|--|------|--------|-------|-----------------------------------|
| | Life Stage Zebrafish: Effects of pH and Intermittent Pulse Exposure | Environmental Safety | | | | |
| Wang, L; Huang, XL; Sun, WL; too, HZ; Laserna, AKC; Li, SFY | A Global Metabolomic Insight into the Oxidative Stress and Membrane Damage of Copper Oxide Nanoparticles and Microparticles on Microalga <i>Chlorella Vulgaris</i> | Environmental Pollution | 2020 | 256 | | 10.1016/j.envpol.2019.113647 |
| Razmara, P; Sharpe, J; Pyle, GG | Rainbow Trout (<i>Oncorhynchus Mykiss</i>) Chemosensory Detection of and Reactions to Copper Nanoparticles and Copper Ions | Environmental Pollution | 2020 | 260 | | 10.1016/j.envpol.2020.113925 |
| Mani, R; Balasubramanian, S; Raghunath, A; Perumal, E | Chronic Exposure to Copper Oxide Nanoparticles Causes Muscle Toxicity in Adult Zebrafish | Environmental Science and Pollution Research | 2020 | 27 | 22 | 10.1007/s11356-019-06095-w |
| Lee, CY; Horng, JL; Liu, ST; Lin, LY | Exposure to Copper Nanoparticles Impairs Ion Uptake, and Acid and Ammonia Excretion by Ionocytes in Zebrafish Embryos | Chemosphere | 2020 | 261 | | 10.1016/j.chemosphere.2020.128051 |

Table S5. Final list of publications used in meta-analysis ($n = 29$), with value assigned to each of the three pillars.

| Authors | Title | Year | DOI | Pillar 1 | Pillar 2 | Pillar 3 |
|---|---|------|-----------------------------------|----------|----------|----------|
| Shi, JY; Abid, AD; Kennedy, IM; Hristova, KR; Silk, WK | To Duckweeds (<i>Landoltia Punctata</i>), Nanoparticulate Copper Oxide Is More Inhibitory Than the Soluble Copper in the Bulk Solution | 2011 | 10.1016/j.envpol.2011.01.028 | 0.67 | 0.80 | 2.00 |
| Pradhan, A; Seena, S; Pascoal, C; Cassio, F | Copper Oxide Nanoparticles Can Induce Toxicity to the Freshwater Shredder <i>Allogamus Ligonifer</i> | 2012 | 10.1016/j.chemosphere.2012.06.001 | 1.00 | 0.60 | 2.33 |
| Manusadzianas, L; Caillet, C; Fachetti, L; Gylte, B; Grigutyte, R; Jurkoniene, S; Karionas, R; Sadauskas, K; Thomas, F; Vitkus, R; Ferard, JF | Toxicity of Copper Oxide Nanoparticle Suspensions to Aquatic Biota | 2012 | 10.1002/etc.715 | 0.67 | 0.40 | 2.00 |
| Pang, CF; Selck, H; Banta, GT; Misra, SK; Berhanu, D; Dybowska, A; Valsami-Jones, E; Forbes, VE | Bioaccumulation, Toxicokinetics, and Effects of Copper from Sediment Spiked with Aqueous Cu, Nano-Cuo, Or Micro-Cuo in the Deposit-Feeding Snail, <i>Potamopyrgus Antipodarum</i> | 2013 | 10.1002/etc.2216 | 0.00 | 1.20 | 2.00 |
| Perreault, F; Samadani, M; Dewez, D | Effect of Soluble Copper Released from Copper Oxide Nanoparticles Solubilisation on Growth and Photosynthetic Processes of <i>Lemna Gibba L.</i> | 2014 | 10.3109/17435390.2013.789936 | 1.00 | 0.40 | 2.00 |
| Rossetto, ALDF; Vicentini, DS; Costa, CH; Melegari, SP; Matias, WG | Synthesis, Characterization and Toxicological Evaluation of a Core-Shell Copper Oxide/Polyaniline Nanocomposite | 2014 | 10.1016/j.chemosphere.2014.03.038 | 0.00 | 0.60 | 2.33 |
| Sankar, R; Prasath, BB; Nandakumar, R; Santhanam, P; Shivashangari, KS; Ravikumar, V | Growth Inhibition of Bloom Forming Cyanobacterium <i>Microcystis Aeruginosa</i> by Green Route Fabricated Copper Oxide Nanoparticles | 2014 | 10.1007/s11356-014-3362-1 | 0.67 | 0.20 | 1.33 |
| Han, X; Geller, B; Moniz, K; Das, P; Chippindale, AK; Walker, VK | Monitoring the Developmental Impact of Copper and Silver Nanoparticle Exposure in <i>Drosophila</i> and their Microbiomes | 2014 | 10.1016/j.scitotenv.2013.12.129 | 1.00 | 0.20 | 2.67 |
| Son, J; Vavra, J; Forbes, VE | Effects of Water Quality Parameters on Agglomeration and Dissolution of Copper Oxide Nanoparticles (CuO-NPs) Using a Central Composite Circumscribed Design | 2015 | 10.1016/j.scitotenv.2015.03.093 | 0.67 | 1.20 | 0.00 |
| Reyes, VC; Opot, SO; Mahendra, S | Planktonic and Biofilm-Grown Nitrogen-Cycling Bacteria Exhibit Different Susceptibilities to Copper Nanoparticles | 2015 | 10.1002/etc.2867 | 0.67 | 0.80 | 2.67 |
| Pradhan, A; Seena, S; Schlosser, D; Gerth, K; Helm, S; Dobritzsch, M; Krauss, GJ; Dobritzsch, D; Pascoal, C; Cassio, F | Fungi from Metal-Polluted Streams May Have High Ability to Cope with the Oxidative Stress Induced by Copper Oxide Nanoparticles | 2015 | 10.1002/etc.2879 | 0.67 | 0.40 | 2.00 |

Table S5. Final list of publications used in meta-analysis ($n = 29$), with value assigned to each of the three pillars.

| Authors | Title | Year | DOI | Pillar 1 | Pillar 2 | Pillar 3 |
|---|--|------|-----------------------------------|----------|----------|----------|
| Son, J; Vavra, J; Li, YS; Seymour, M; Forbes, V | Interactions Between Suspension Characteristics and Physicochemical Properties of Silver and Copper Oxide Nanoparticles: A Case Study for Optimizing Nanoparticle Stock Suspensions Using a Central Composite Design | 2015 | 10.1016/j.chemosphere.2014.12.005 | 0.67 | 0.20 | 0.00 |
| Regier, N; Cosio, C; von Moos, N; Slaveykova, VI | Effects of Copper-Oxide Nanoparticles, Dissolved Copper and Ultraviolet Radiation on Copper Bioaccumulation, Photosynthesis and Oxidative Stress in the Aquatic Macrophyte <i>Elodea Nuttallii</i> | 2015 | 10.1016/j.chemosphere.2014.12.078 | 0.67 | 0.80 | 2.67 |
| Muller, E; Behra, R; Sigg, L | Toxicity of Engineered Copper (Cu-0) Nanoparticles to the Green Alga <i>Chlamydomonas Reinhardtii</i> | 2016 | 10.1071/EN15130 | 1.00 | 1.00 | 2.33 |
| Ostaszewska, T; Chojnacki, M; Kamaszewski, M; Sawosz-Chwalibog, E | Histopathological Effects of Silver and Copper Nanoparticles on the Epidermis, Gills, And Liver Of Siberian Sturgeon | 2016 | 10.1007/s11356-015-5391-9 | 0.67 | 2.60 | 2.33 |
| Wang, Z; Fang, H; Wang, S | Benzoic Acid Interactions Affect Aquatic Properties and Toxicity of Copper Oxide Nanoparticles | 2016 | 10.1007/s00128-016-1804-9 | 0.67 | 0.80 | 2.33 |
| Black, MN; Henry, EF; Adams, OA; Bennett, JCF; MacCormack, TJ | Environmentally Relevant Concentrations of Amine-Functionalized Copper Nanoparticles Exhibit Different Mechanisms of Bioactivity in <i>Fundulus Heteroclitus</i> in Fresh and Brackish Water | 2017 | 10.1080/17435390.2017.1395097 | 1.00 | 2.20 | 2.33 |
| Thit, A; Huggins, K; Selck, H; Baun, A | Acute Toxicity of Copper Oxide Nanoparticles to <i>Daphnia Magna</i> Under Different Test Conditions | 2017 | 10.1080/02772248.2016.1249368 | 1.00 | 1.20 | 2.00 |
| Liu, YX; Yan, ZH; Xia, J; Wang, K; Ling, XC; Yan, B | Potential Toxicity in Crucian Carp Following Exposure to Metallic Nanoparticles of Copper, Chromium, and their Mixtures: A Comparative Study | 2017 | 10.15244/pjoes/69251 | 0.00 | 1.60 | 2.33 |
| Vicario-Pares, U; Lacave, JM; Reip, P; Cajaraville, MP; Orbea, A | Cellular and Molecular Responses of Adult Zebrafish After Exposure to CuO Nanoparticles or Ionic Copper | 2018 | 10.1007/s10646-017-1873-5 | 1.00 | 0.60 | 2.67 |
| Xiao, YL; Peijnenburg, WJGM; Chen, GC; Vijver, MG | Impact of Water Chemistry on the Particle-Specific Toxicity of Copper Nanoparticles to <i>Daphnia Magna</i> | 2018 | 10.1016/j.scitotenv.2017.08.188 | 1.00 | 1.00 | 2.00 |
| Braz-Mota, S; Campos, DF; MacCormack, TJ; Duarte, RM; Val, AL; Almeida-Val, VMF | Mechanisms of Toxic Action of Copper and Copper Nanoparticles in Two Amazon Fish Species: Dwarf Cichlid (<i>Apistogramma Agassizii</i>) and Cardinal Tetra (<i>Paracheirodon Axelrodi</i>) | 2018 | 10.1016/j.scitotenv.2018.02.216 | 1.00 | 0.80 | 2.33 |

Table S5. Final list of publications used in meta-analysis ($n = 29$), with value assigned to each of the three pillars.

| Authors | Title | Year | DOI | Pillar 1 | Pillar 2 | Pillar 3 |
|---|--|------|-----------------------------------|-------------|-------------|-------------|
| Yang, L; Wang, WX | Comparative Contributions of Copper Nanoparticles and Ions to Copper Bioaccumulation and Toxicity in Barnacle Larvae | 2019 | 10.1016/j.envpol.2019.02.103 | 1.00 | 1.60 | 2.00 |
| Miao, LZ; Wang, PF; Hou, J; Yao, Y; Liu, ZL; Liu, SQ | Low Concentrations of Copper Oxide Nanoparticles Alter Microbial Community Structure and Function of Sediment Biofilms | 2019 | 10.1016/j.scitotenv.2018.10.354 | 1.00 | 2.20 | 3.00 |
| Parsai, T; Kumar, A | Understanding Effect of Solution Chemistry on Heteroaggregation of Zinc Oxide and Copper Oxide Nanoparticles | 2019 | 10.1016/j.chemosphere.2019.06.171 | 1.00 | 0.80 | 0.00 |
| Kansara, K; Paruthi, A; Misra, SK; Karakoti, AS; Kumar, A | Montmorillonite Clay and Humic Acid Modulate the Behavior of Copper Oxide Nanoparticles in Aqueous Environment and Induces Developmental Defects in Zebrafish Embryo | 2019 | 10.1016/j.envpol.2019.113313 | 0.67 | 1.00 | 2.67 |
| Mani, R; Balasubramanian, S; Raghunath, A; Perumal, E | Chronic Exposure to Copper Oxide Nanoparticles Causes Muscle Toxicity in Adult Zebrafish | 2020 | 10.1007/s11356-019-06095-w | 0.33 | 0.20 | 2.67 |
| Boyle, D; Clark, NJ; Handy, RD | Toxicities of Copper Oxide Nanomaterial and Copper Sulphate in Early Life Stage Zebrafish: Effects of pH and Intermittent Pulse Exposure | 2020 | 10.1016/j.ecoenv.2019.109985 | 0.67 | 1.00 | 2.33 |
| Razmara, P; Sharpe, J; Pyle, GG | Rainbow Trout (<i>Oncorhynchus Mykiss</i>) Chemosensory Detection of and Reactions to Copper Nanoparticles and Copper Ions | 2020 | 10.1016/j.envpol.2020.113925 | 0.67 | 1.80 | 2.33 |
| Mean | | | | 0.72 | 0.97 | 2.06 |