«*Ut sementem feceris, ita metes*» plastic, pesticides, and human health?

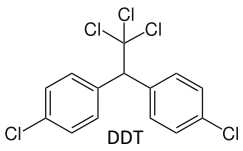
LASC special series

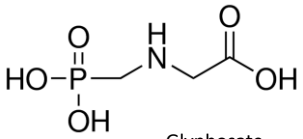
February 2022

Marc Emmenegger

Introduction

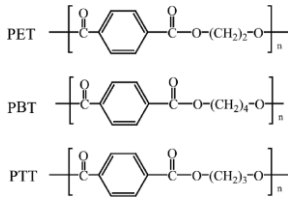
Product





Glyphosate

PET

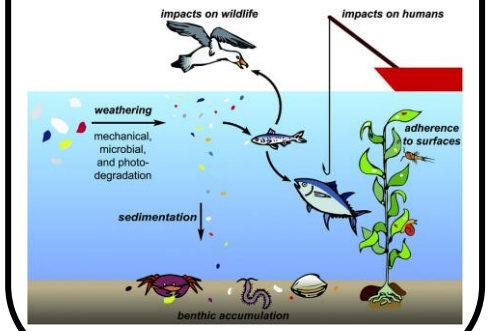


Initial testing/safety

LD50

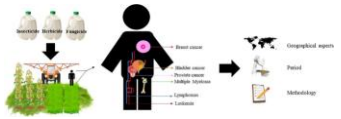
- Agricultural products are tested in cell culture systems and in mice.
- Not in humans – no clinical trials, not used to treat humans.
- Just because they are clearly toxic at high concentrations does not mean they are bad.
- Plastic: a product of the human era of convenience. Not primarily considered relevant to health, not supposed to end up in food chain as microplastic…

Effect on ecosystem



Direct and **indirect** effects

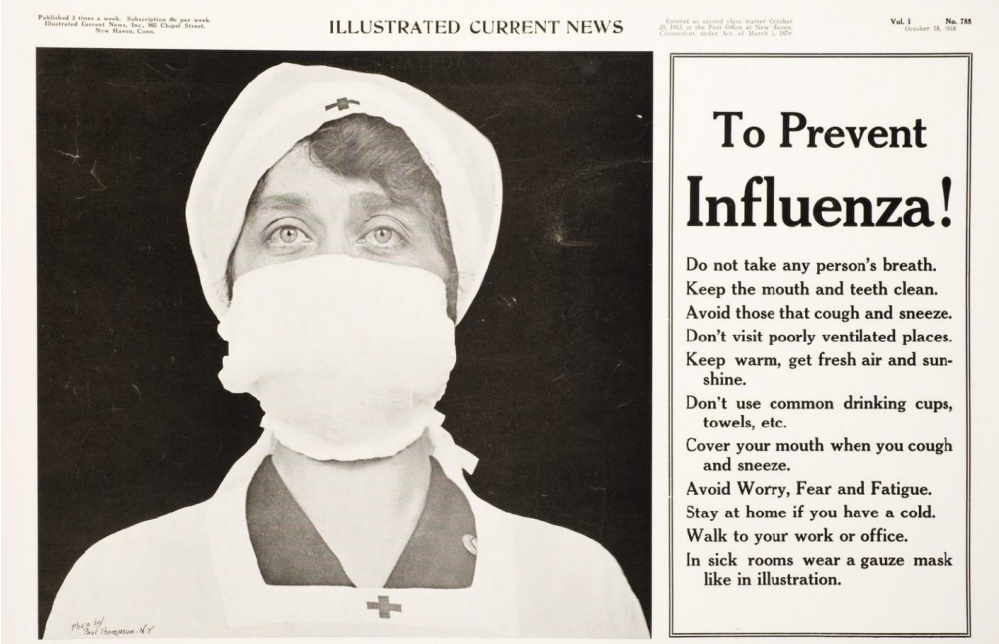
Effect on human health



- **Concentration/route**. Acute poisoning, ingestion/ inhalation/ dermal contact.
- **Occupational** versus **consumer**.
- **Unifactorial** (a single agent was studied and is harmless) versus **multifactorial** (single agents act together, not studied).
- **Deterministic** (easy to assess) versus **stochastic** (hard to identify).
- **Short-term** consequences (e.g. skin rash) **versus long-term** consequences (e.g. disease manifests at old age, cancer in next generation, …).

Choice of JC topic

- Curiosity – wish to understand more.
- Fact/ke – what is scientifically known, what is blatant esotericism (many stakeholders)?
- Interest in epidemiological research/public health that goes beyond infectious disease.



New Haven, 1918

Choice of JC topic

- Curiosity – wish to understand more.
- Fact/ke – what is scientifically known, what is blatant esotericism (many stakeholders)?
- Interest in epidemiological research/public health that goes beyond infectious disease.

Pesticides/microplastic

1. What are they?
2. What are some of the claims regarding the effect of pesticides/microplastic on human health?
3. What evidence do we have to support such claims?

1. What are pesticides?

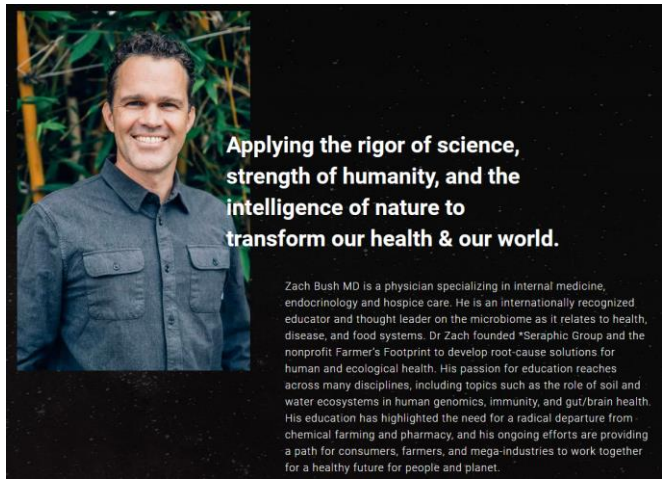
- Pesticides are chemical compounds that are **used to kill pests**, including **insects**, **rodents**, **fungi** and **unwanted plants** (weeds).
- Over 1000 different pesticides are used around the world.
- By their nature, pesticides are **potentially toxic to other organisms**, including humans, and need to be used safely and disposed of properly.
- Many of the older, cheaper (off-patent) pesticides, such as dichlorodiphenyltrichloroethane (**DDT**) and **lindane**, **can remain for years in soil and water**.
- These have adverse effects on larger parts of the ecosystem and can accumulate in the food chain. These chemicals have been banned by countries who signed the 2001 Stockholm Convention.

Type	Action
Algicides	Control algae in lakes, canals, swimming pools, water tanks, and other sites
Antifouling agents	Kill or repel organisms that attach to underwater surfaces, such as boat bottoms
Antimicrobials	Kill microorganisms (such as bacteria and viruses)
Attractants	Attract pests (for example, to lure an insect or rodent to a trap). (However, food is not considered a pesticide when used as an attractant.)
Biopesticides	Biopesticides are certain types of pesticides derived from such natural materials as animals, plants, bacteria, and certain minerals
Biocides	Kill microorganisms
Disinfectants and sanitizers	Kill or inactivate disease-producing microorganisms on inanimate objects
Fungicides	Kill fungi (including blights, mildews, molds, and rusts)
Fumigants	Produce gas or vapor intended to destroy pests in buildings or soil
Herbicides	Kill weeds and other plants that grow where they are not wanted
Insecticides	Kill insects and other arthropods
Miticides	Kill mites that feed on plants and animals
Microbial pesticides	Microorganisms that kill, inhibit, or out compete pests, including insects or other microorganisms
Molluscicides	Kill snails and slugs
Nematicides	Kill nematodes (microscopic, worm-like organisms that feed on plant roots)
Ovicides	Kill eggs of insects and mites
Pheromones	Biochemicals used to disrupt the mating behavior of insects
Repellents	Repel pests, including insects (such as mosquitoes) and birds
Rodenticides	Control mice and other rodents
Slimicides	Kill slime-producing microorganisms such as algae, bacteria, fungi, and slime molds

WHO

Wikipedia

2. Pesticides and human health: What some people claim



- Pesticide-Induced Diseases Database
  - Overview
  - Search the Database
  - Asthma and Respiratory Effects
  - Birth Defects
  - Body Burden
  - Brain and Nervous System Disorders
  - Cancer
  - Diabetes
  - Endocrine Disruption
  - Immune System Disorders
  - Learning/Developmental
  - Sexual and Reproductive Dysfunction

Alzheimer's Disease • Amyotrophic Lateral Sclerosis (ALS) • Dementia • Epilepsy & Seizures • Multiple Sclerosis (MS) • Parkinson's Disease • Other Neurological & Nervous System Disturbances

Arthritis/Osteoporosis • Celiac Disease • Hepatitis • Hypersensitivity • Lupus • Multiple Sclerosis

SHOP NOW

B.Smart Brain Fuel

SHOP NOW

ION* Gut Support

All natural and soil derived, ION* Gut Support goes beyond probiotics to defend you from environmental toxins and diversify your gut microbiome naturally.

SHOP NOW

ION* Skin Support

ION* Skin Support spray defends against toxins and facilitates microbial connection, helping to reduce redness and signs of skin damage while also encouraging skin to breathe and glow.

SHOP NOW

ION* Sinus Support

ION* Sinus Support is a non-habit forming and all natural nasal spray, facilitating the innate connection between you and your microbiome. This helps to soothe and protect your nasal passages while also allowing you to breathe clearly and maintain natural hydration.

SHOP NOW

ION* Gut Support For Pets

All natural and soil derived, ION* Gut Support For Pets supplement helps to defend your furry family members from environmental toxins and diversify their microbiome.

3. Pesticides and human health: What evidence do we have?

Published: December 2000

Chronic systemic pesticide exposure reproduces features of Parkinson's disease

Ranjita Betarbet, Todd B. Sherer, Gillian MacKenzie, Monica Garcia-Osuna, Alexander V. Panov & J. Timothy Greenamyre

Nature Neuroscience **3**, 1301–1306 (2000) | Cite this article

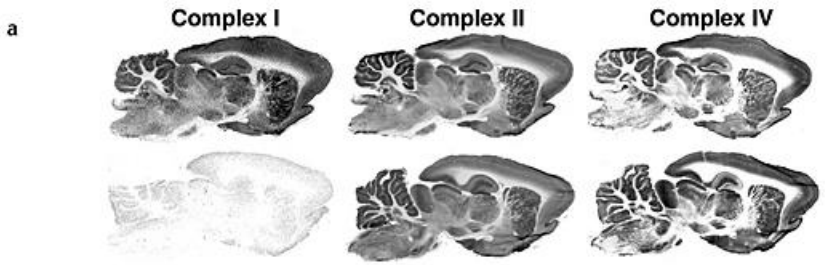
- Epidemiological studies have suggested that pesticide exposure is associated with an increased risk of developing PD.
- The pro-toxin N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (**MPTP**) was reported to produce in humans an acute parkinsonian syndrome that is virtually indistinguishable from idiopathic PD.
- Its metabolite, 1-methyl-4-pyridinium (**MPP+),** was found to be a mitochondrial poison.
- The selectivity of MPP+ for dopaminergic neurons is due to the fact that it is an excellent substrate for the dopamine transporter.
- They exposed rats chronically, continuously and systemically to the common pesticide, **rotenone**.
- A naturally occurring compound derived from the roots of certain plant species, rotenone is commonly used as an insecticide in vegetable gardens, and is also used to kill or sample fish populations in lakes and reservoirs.
- Because it is extremely hydrophobic, rotenone crosses biological membranes easily, and it does not depend on the dopamine transporter for access to the cytoplasm. Therefore, rotenone—unlike MPTP—is well-suited to produce a systemic inhibition of complex I.

Chronic systemic pesticide exposure reproduces features of Parkinson's disease

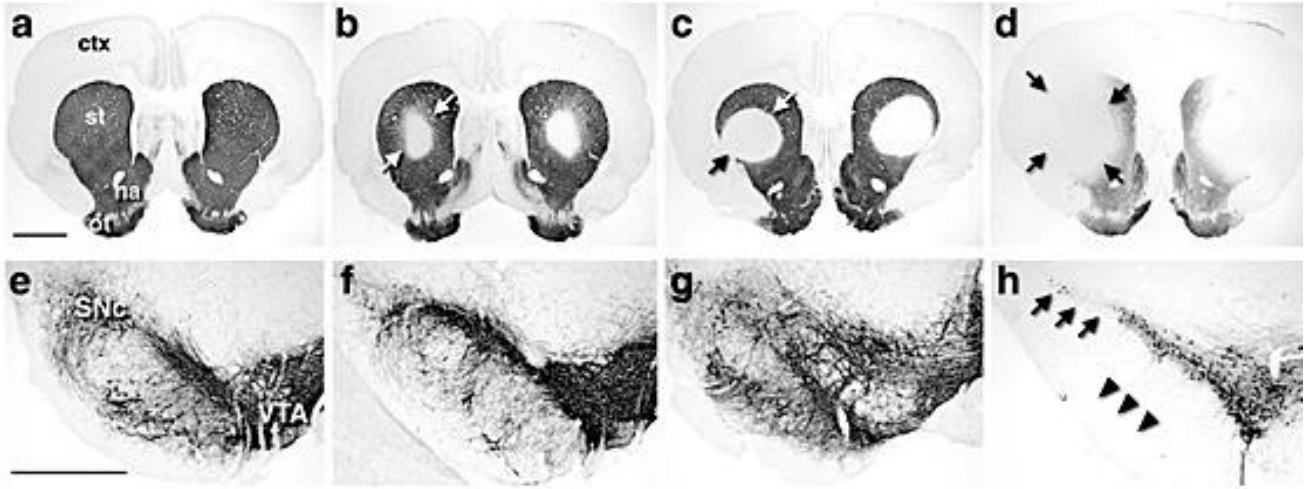
- 2.0 mg/kg per day for 2 days.
- Histochemical analysis of mitochondrial complexes.
- [3H]dihydrorotenone binding to complex I in brain was reduced by about 75%.

- Progressive striatal dopaminergic denervation (arrows), ranging from partial (b, c) to almost complete (d) was observed.
- Systemic rotenone infusion resulted in nigrostriatal dopaminergic degeneration.

Figure 1: Rotenone infusion selectively and uniformly affected complex I throughout the brain.



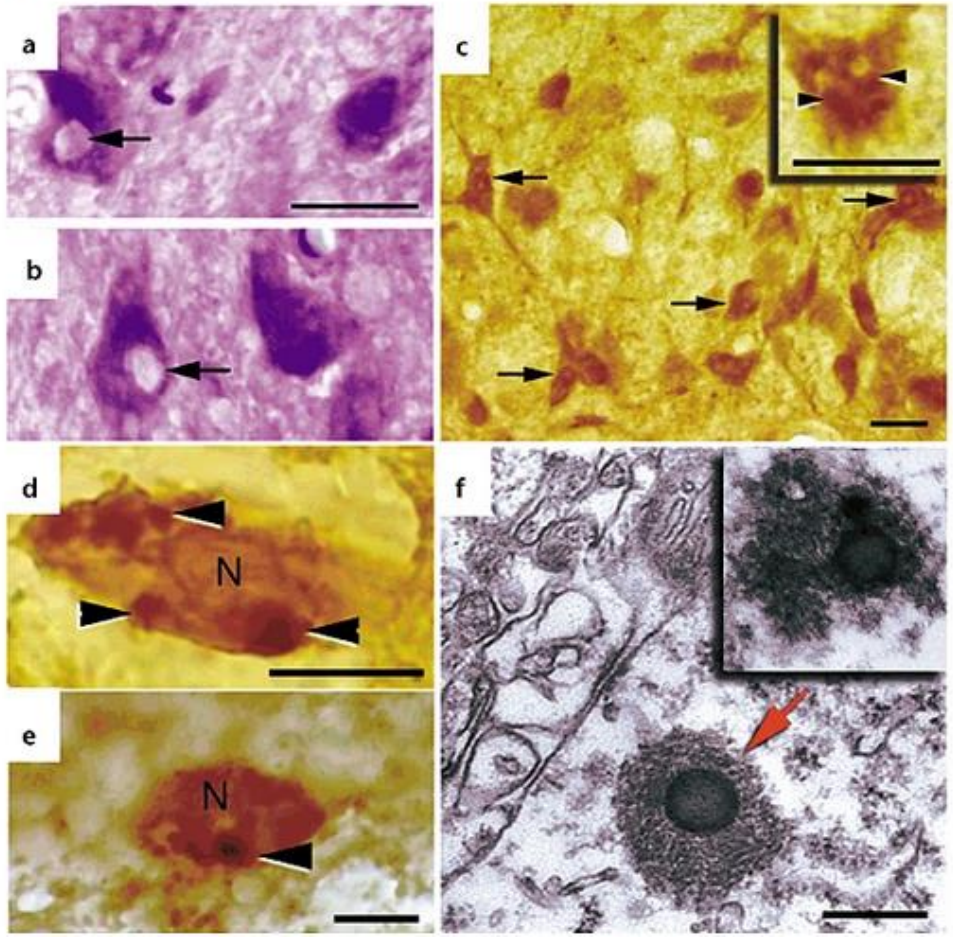
Ctrl. Rotenone



Chronic systemic pesticide exposure reproduces features of Parkinson's disease

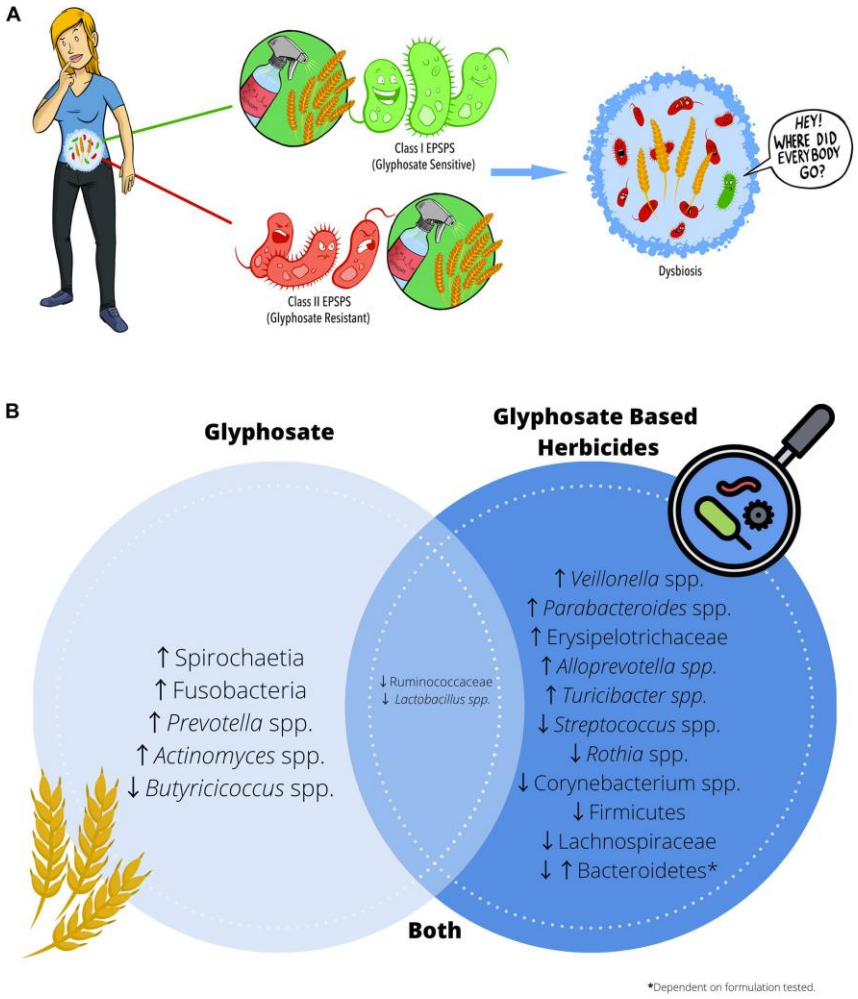
- (a, b) Pale cytoplasmic inclusions (arrows) were seen in nigral neurons of rotenone-infused rats by standard hematoxylin and eosin staining. Scale bar, 25 µm.
- (c) Cytoplasmic inclusions in nigral neurons contained ubiquitin immunoreactivity. Arrows indicate cells containing ubiquitin-positive aggregates. Inset, a nigral cell at higher magnification illustrating ubiquitin-positive inclusions (arrowheads). Scale bars, 25 µm.
- (d, e) Neurons with α-synuclein-positive inclusions (arrowheads) Scale bars, 10 µm. N, nucleus.
- (f) Ultrastructural analysis of inclusions showed a dense core with peripheral fibrillar elements (arrow). Inset, an α-synuclein-positive inclusion as demonstrated by immuno-electron microscopy. Scale bar, 1 µm.
- Rotenone-treated animals developed motor and postural deficits characteristic of PD.
- All animals with a dopaminergic lesion became hypokinetic and had unsteady movement and hunched posture, even after termination of the rotenone infusion.
- However, rotenone seems to have little toxicity when administered orally.
- **22 years later, rotenone is still widely used…**

Figure 5: Cytoplasmic inclusions in nigral neurons of rotenone-infused rats.



Observations I

- The situation is complex.
- A generally negative impact on biodiversity/the environment/soil quality is usually agreed on.
  - Not just by the scientific community.
  - Apparently more and more also among agricultural scientists and farmers themselves.
- There is an occupational hazard, as with many professions (scientists, cleaning personal, …).
- The effect of many different pesticides on human health through the food chain/water is questionable.
- Data is often ambiguous.
- As long as data is ambiguous, possibly illicit and sometimes criminal claims have a lot of fertile ground to grow.



Glyphosate inhibits the shikimate pathway, a pathway exclusive to plants and bacteria. Glyphosate's effect on dysbiosis was not considered when making safety recommendations.

Barnett, Gibson, Front. Microbiol. 2020.

Observations II

nature > nature plants > comment > article

Comment | Published: 14 October 2021

No pesticide-free Switzerland

Robert Finger

Nature Plants **7**, 1324–1325 (2021) | Cite this article

On 13 June 2021, the people of Switzerland voted on two popular initiatives that aimed to introduce stricter pesticide policies. Both initiatives were rejected, but the political and societal debate led to large changes in governmental and industry policies.

Pest management is critical for food security and the provision of various ecosystem services from the agricultural sector[1]. However, the use of pesticides has negative effects on human health and the environment[2,3]. Many countries have placed the reduction of pesticide risks

Observations III

RESEARCH | Open Access | Published: 14 January 2019

How did the US EPA and IARC reach diametrically opposed conclusions on the genotoxicity of glyphosate-based herbicides?

Charles M. Benbrook

Environmental Sciences Europe **31**, Article number: 2 (2019) | Cite this article

33k Accesses | **56** Citations | **396** Altmetric | Metrics

- The **US EPA** considers glyphosate as "**not likely to be carcinogenic to humans**."
- The International Agency for Research on Cancer (**IARC**) has classified glyphosate as "**probably carcinogenic to humans** (Group 2A)."
- Why and how did EPA and IARC reach such different conclusions?
  - They considered different studies (technical assessments versus academic).
  - They looked at different target populations: consumer hazards or occupational hazards.

HOME > COMMENTARY > BLOGS > IN THE PIPELINE > GLYPHOSATE AND CANCER

IN THE PIPELINE | CANCER

Glyphosate And Cancer

18 MAY 2016 · BY DEREK LOWE · 7 MIN READ · COMMENTS

- UN I: **World Health Organization** and **the Food and Agriculture Organization** have come out with a statement that glyphosate is "**unlikely to pose a carcinogenic risk in humans**".
- UN II: **International Agency for Research on Cancer**, stated what looks like the exact opposite, that it **could "probably" be a cause of cancer in humans**.
- Sharks are a hazard
  - But for most people, they never pose a real risk.
  - The risk becomes real when you swim in shark bay while bleeding.
  - The risk is low in the car in front of the aquarium.
  - And although it is still low, it is increased (e.g. by a factor of 1,000,000) if you enter the aquarium.
  - But it is not relevant in real life.

nature > letters > article

Published: 09 July 2014

Declines in insectivorous birds are associated with high neonicotinoid concentrations

Caspar A. Hallmann, Ruud P. B. Foppen, Chris A. M. van Turnhout, Hans de Kroon & Eelke Jongejans

Nature **511**, 341–343 (2014) | Cite this article

Neonicotinoids and decline in bird biodiversity in the United States

Yijia Li, Ruiqing Miao & Madhu Khanna

Nature Sustainability **3**, 1027–1035 (2020) | Cite this article

A Common Pesticide Decreases Foraging Success and Survival in Honey Bees

MICKAËL HENRY , MAXIME BÉGUIN, FABRICE REQUIER, ORIANNE ROLLIN, JEAN-FRANÇOIS ODOUX, PIERRICK AUPINEL, JEAN APTEL, SYLVIE TCHAMITCHIAN, AND AXEL DECOURTYE Authors Info & Affiliations

SCIENCE • 29 Mar 2012 • Vol 336, Issue 6079 • pp. 348-350 • DOI: 10.1126/science.1215039

Neonicotinoid Pesticide Reduces Bumble Bee Colony Growth and Queen Production

PENELOPE R. WHITEHORN, STEPHANIE O'CONNOR, FELIX L. WACKERS, AND , DAVE GOULSON Authors Info & Affiliations

SCIENCE • 29 Mar 2012 • Vol 336, Issue 6079 • pp. 351-352 • DOI: 10.1126/science.1215025

Published: 22 January 2014

Pathogens and insect herbivores drive rainforest plant diversity and composition

Robert Bagchi, Rachel E. Gallery, Sofia Gripenberg, Sarah J. Gurr, Lakshmi Narayan, Claire E. Addis, Robert P. Freckleton & Owen T. Lewis

Nature **506**, 85–88 (2014) | Cite this article

Observations IV

Combinations of different active ingredients are even more understudied.

ARTICLES
https://doi.org/10.1038/s41561-021-00712-5
nature geoscience
Check for updates

Risk of pesticide pollution at the global scale

Fiona H. M. Tang[1], Manfred Lenzen[2], Alexander McBratney[3] and Federico Maggi[1]

- **Agrochemicals** such as synthetic fertilizers and pesticides have together made a **remarkable contribution to food security** in the last 50 years.
- Notwithstanding the increased food availability, the **unpreventable ubiquity of agrochemicals throughout the environment has resulted in pollution and has negatively impacted the ecosystem and human health**.
- The **global repercussions of pesticide dispersion in the environment remain largely unknown** due to the lack of a comprehensive geographic quantification of active ingredient (AI) use and residues.
- Given the expected population growth, the use of agricultural pesticides will probably continue to increase in the future; yet, in the age of globalization, a **global outlook on environmental pollution by pesticides and its relation to ecosystem vulnerability is still missing**.
- Global mapping of the environmental risks posed by the 92 most used AIs (comprising 59 herbicides, 21 insecticides and 19 fungicides) at 5 arcmin resolution (**about 10 km × 10 km at the Equator**).
- Juxtaposed with water scarcity, biodiversity and national income.
- Assessment targets the ecological risks in four environmental compartments (namely soil, surface water, groundwater and atmosphere).
- Pesticide impacts on human health not focused.

Pesticide pollution at global scale

- Predicted environmental concentration for each of the 92 AI and each environmental compartment.
- Georeferenced environmental datasets and AI physicochemical properties as inputs, in addition to PEST-CHEMGRIDSv120 global database (AI application rate).
- Risk quotient was determined as the ratio between the PEC and the predicted no-effect concentration.
- 74.8% of the global agricultural land (approximately 28.8 million km2) is at some risk of pesticide pollution (RS > 0).
- 31.4% (approximately 12.1 million km2) falls within the high-risk class (RS > 3).
- Europe high risk.
- Asia, with China, has globally highest risk.

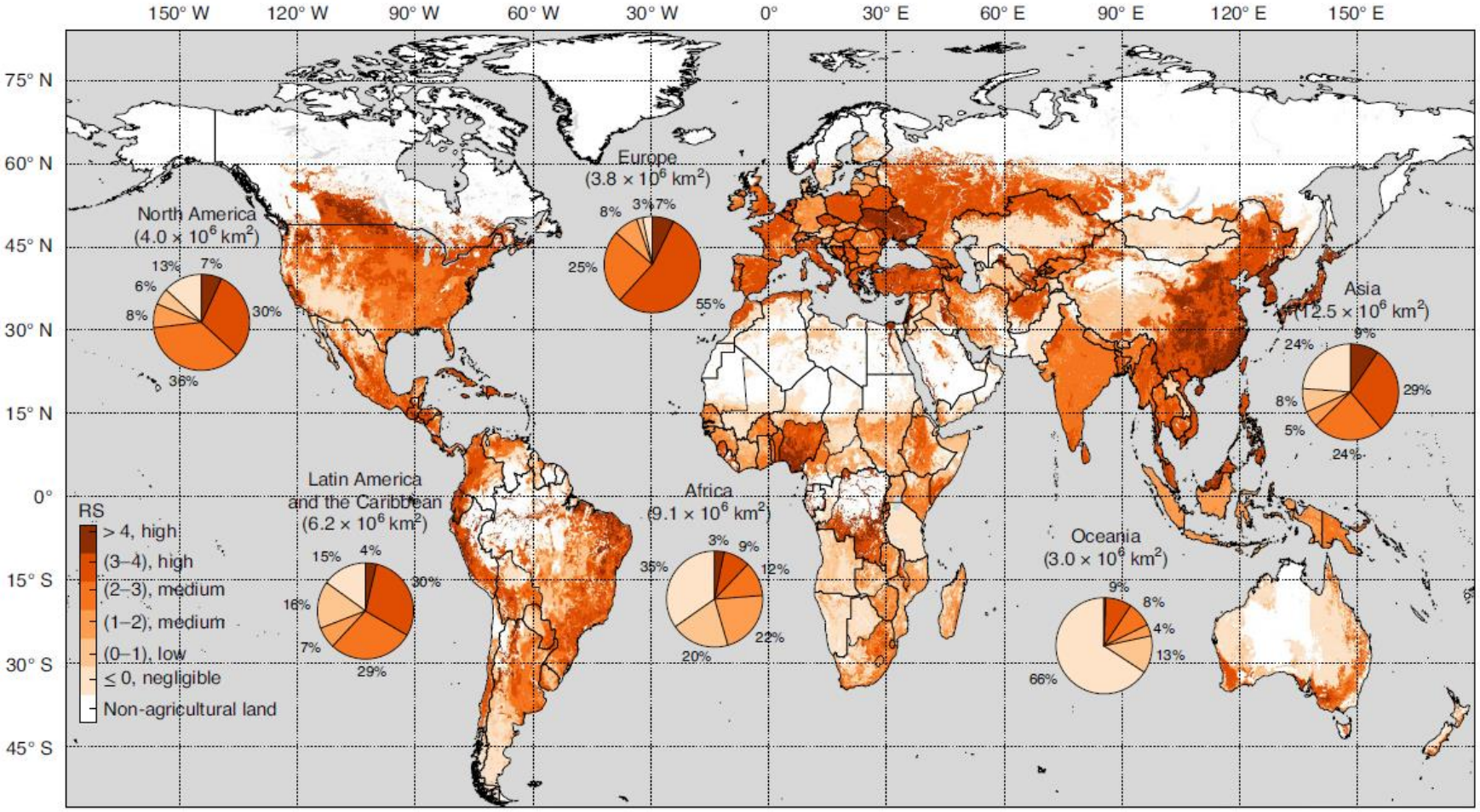


Fig. 1 | Global map of pesticide RS. The map has a spatial resolution of 5 arcmin, which is approximately 10 km × 10 km at the Equator. The pie charts represent the fraction of agricultural land classed under different RS in each region, and the values in parentheses above the pie charts denote the total agricultural land in that region.

Pesticide pollution at global scale

- Pollution by pesticide mixtures is an emerging global issue because **mixtures can elicit synergistic toxicity in non-target organisms** under both acute and chronic exposures.
- 63.7% of the agricultural land is at risk of pollution by more than one AI.
- 20.9% by more than ten AIs.
- 93.7%, 73.4% and 69.4% of the agricultural land in Europe, North America and South America, respectively, is contaminated by more than one AI.
- China is at risk of pollution by the greatest number of AIs, with 8.4% of the agricultural land (0.34 million km2) contaminated by more than 20 AIs.

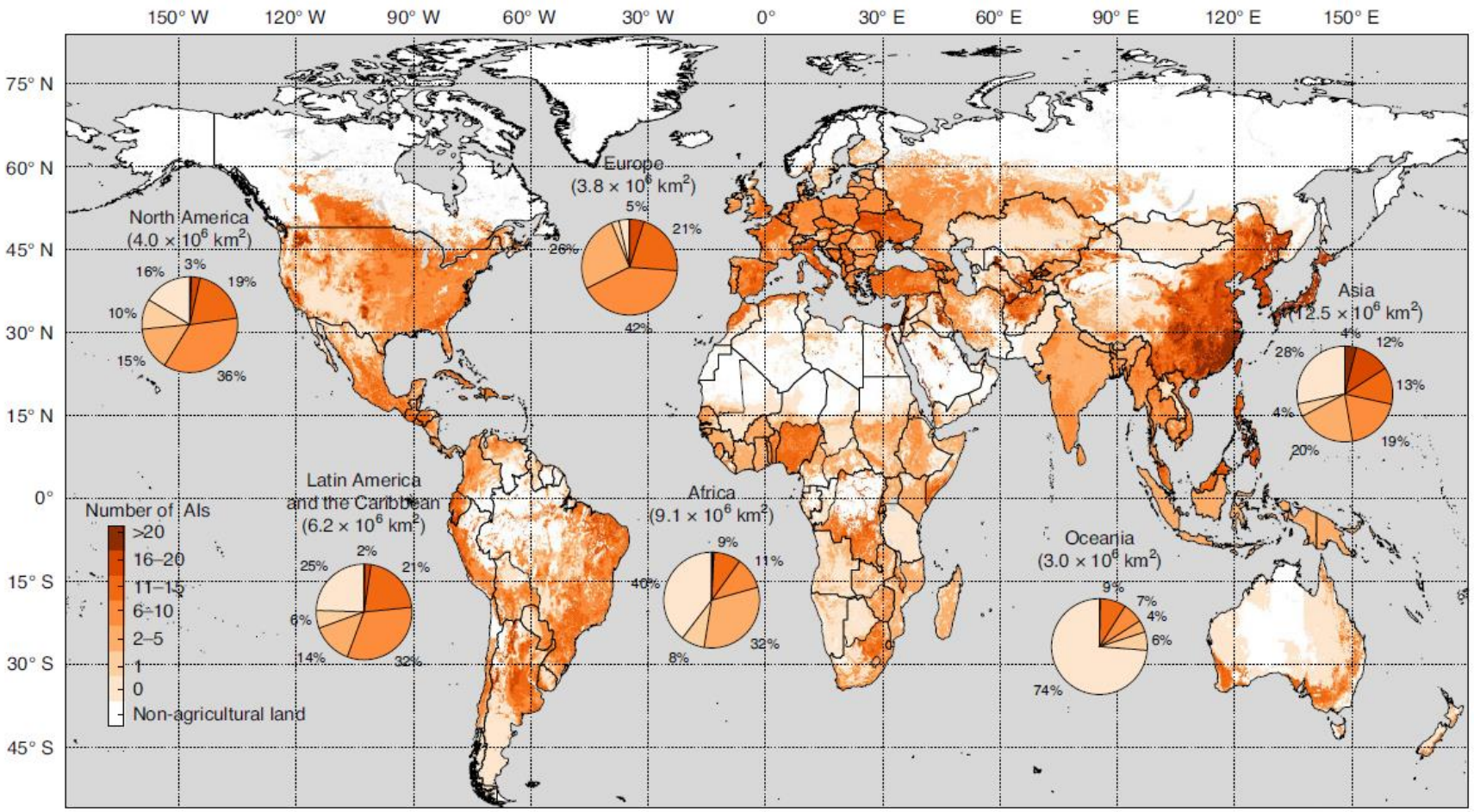


Fig. 2 | Global map of the number of AIs posing risks to the environment. The map has a spatial resolution of 5 arcmin, which is approximately 10 km × 10 km at the Equator. The pie charts represent the fraction of agricultural land contaminated by different numbers of AIs in each region, and the values in parentheses above the pie charts denote the total agricultural land in that region.

Pesticide pollution at global scale

- To provide a synthesis, integration of **pesticide pollution risk**, **water scarcity** and **biodiversity** into a map that locates regions of concern where tailored strategies for the sustainable use of pesticides may be needed.
- Level 1: high pollution risk, high water scarcity and high biodiversity.
- Identified the top five watersheds perceiving a level 1 concern as **Orange in South Africa**, **Huang He in China**, **Indus in India**, **Murray in Australia**, and **Parana in Argentina**.
- Surprisingly, four out of the five countries with level 1 concern are within high and upper-middle-income economies.
- Besides impacting ecosystem health, the leaching of pesticides into water bodies used as sources of drinking water can pose risks to human health.
- Although protecting food production is essential for human development, **reducing pesticide pollution is equivalently crucial to protect the biodiversity that maintains soil health and functions**, contributing towards food security.

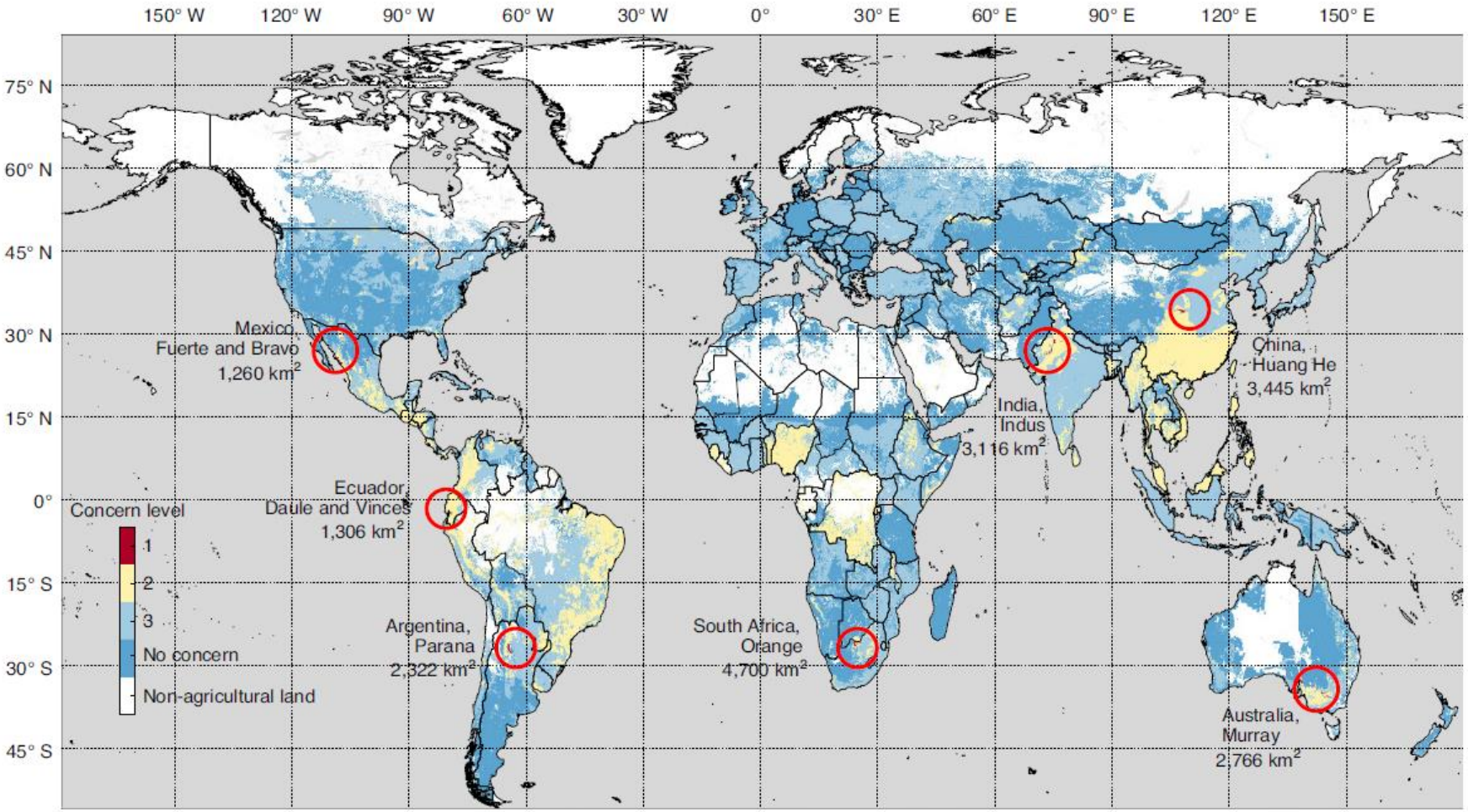
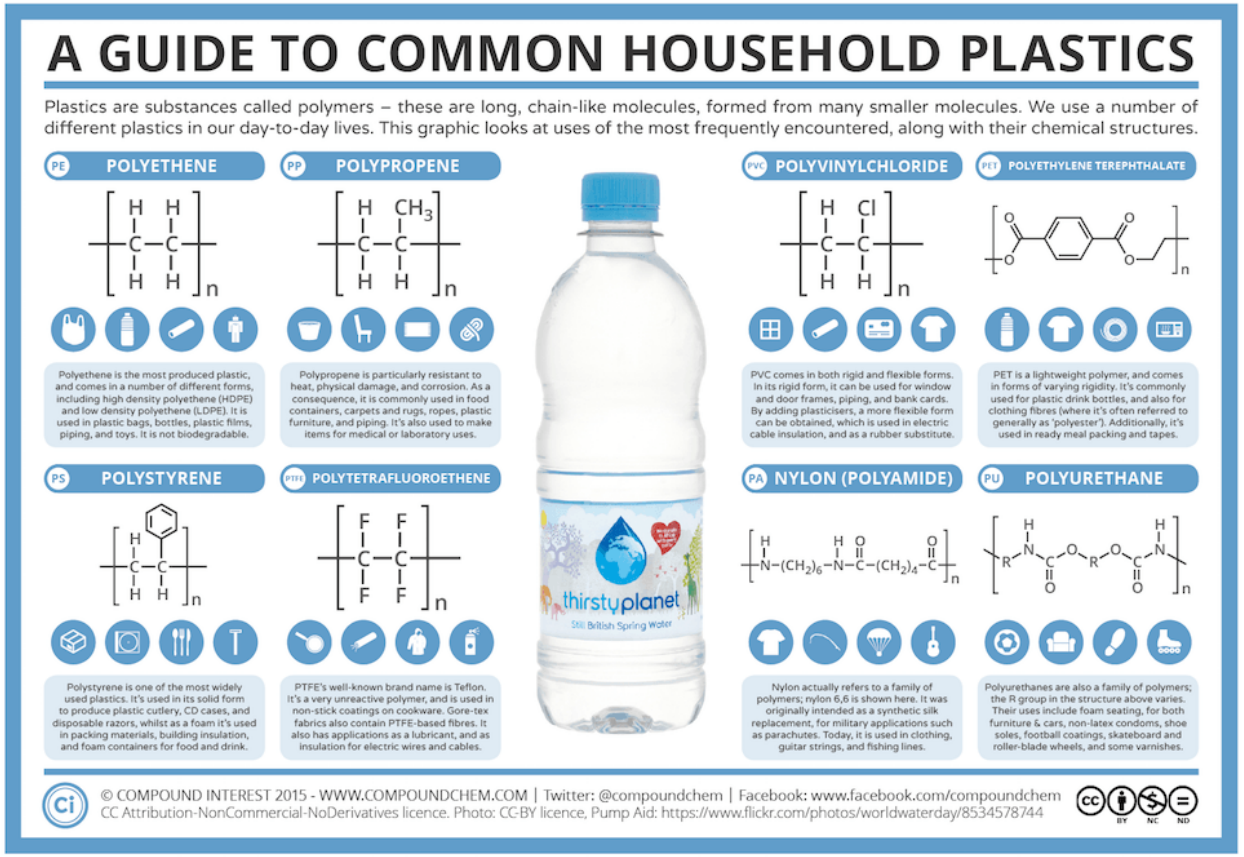
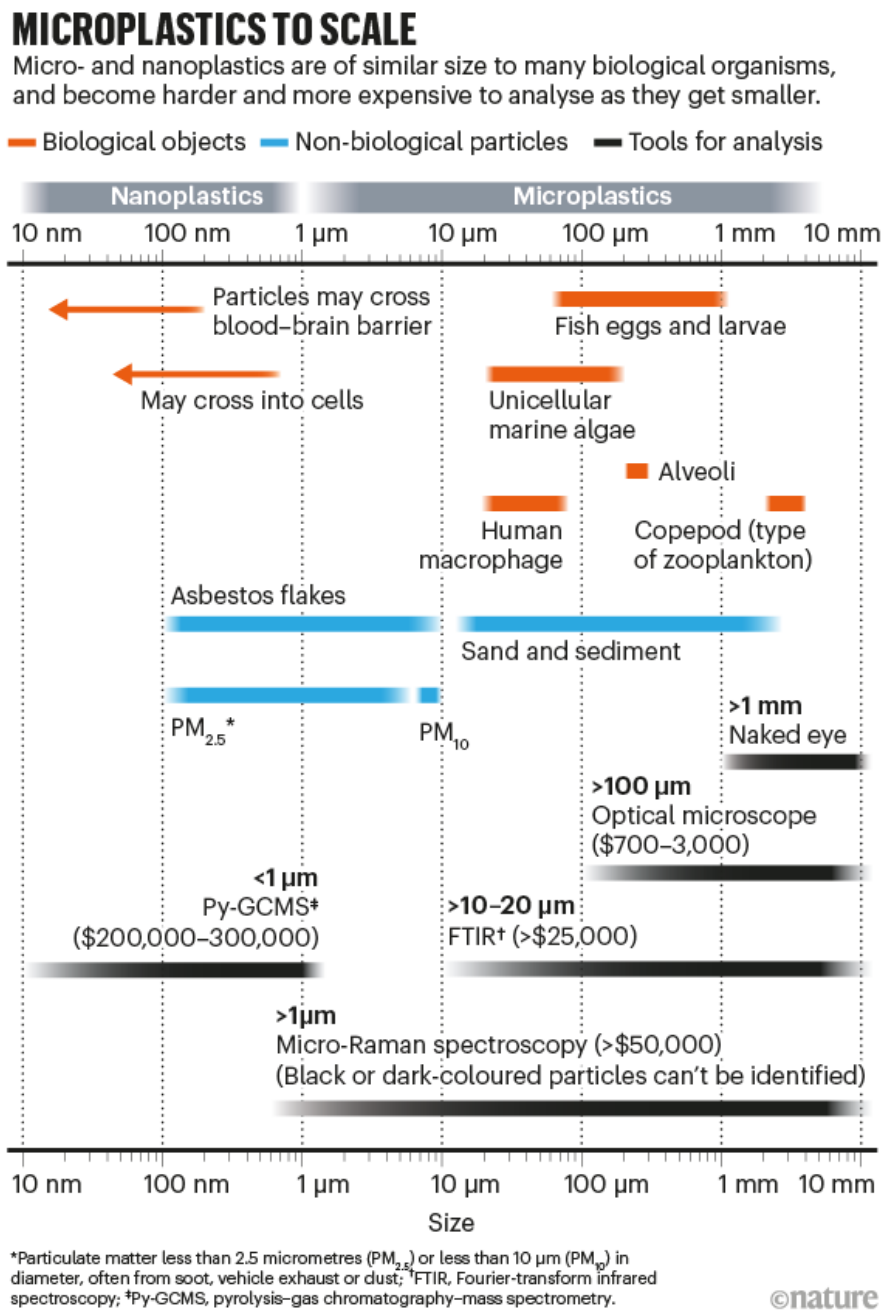


Fig. 3 | Global map of the regions of concern defined by pesticide pollution risk, water scarcity and biodiversity. Regions of level 1 concern are areas of high pesticide pollution risk, high water scarcity and high biodiversity. They are indicated by red circles, with the country, watershed name and area of impacted land listed. The map has a spatial resolution of 5 arcmin, which is approximately 10 km × 10 km at the Equator.

1. What is plastic/microplastic?



Versatile material with different grades and varieties.

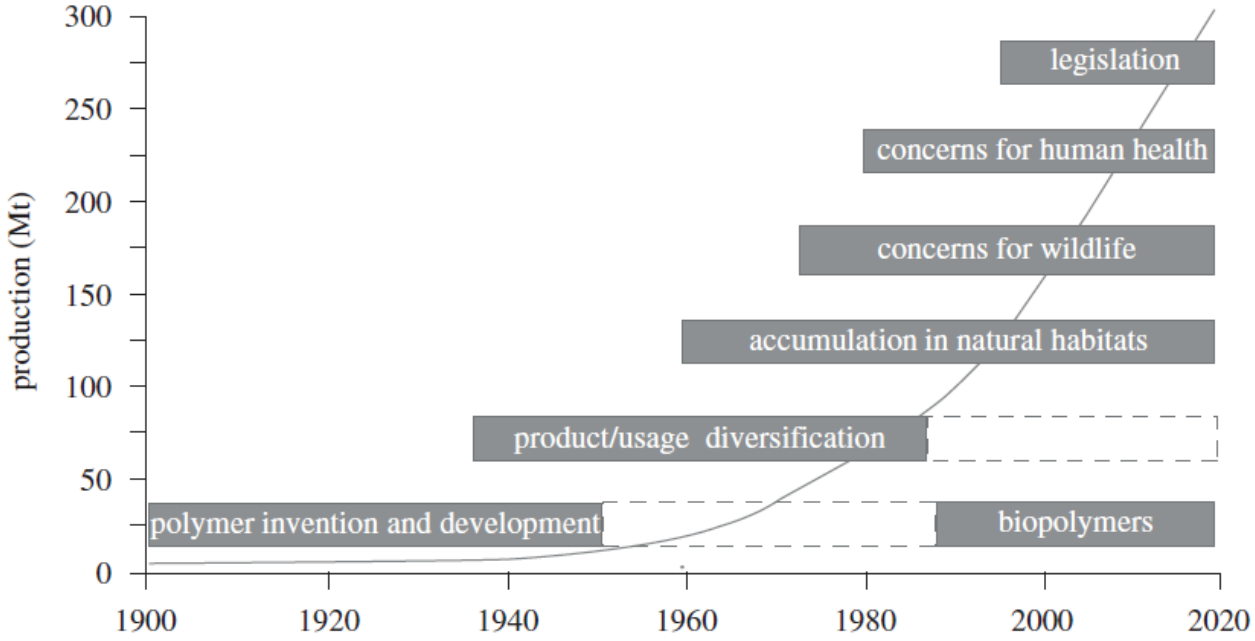


*Particulate matter less than 2.5 micrometres ($PM_{2.5}$) or less than 10 µm (PM_{10}) in diameter, often from soot, vehicle exhaust or dust; †FTIR, Fourier-transform infrared spectroscopy; ‡Py-GCMS, pyrolysis–gas chromatography–mass spectrometry.

©nature

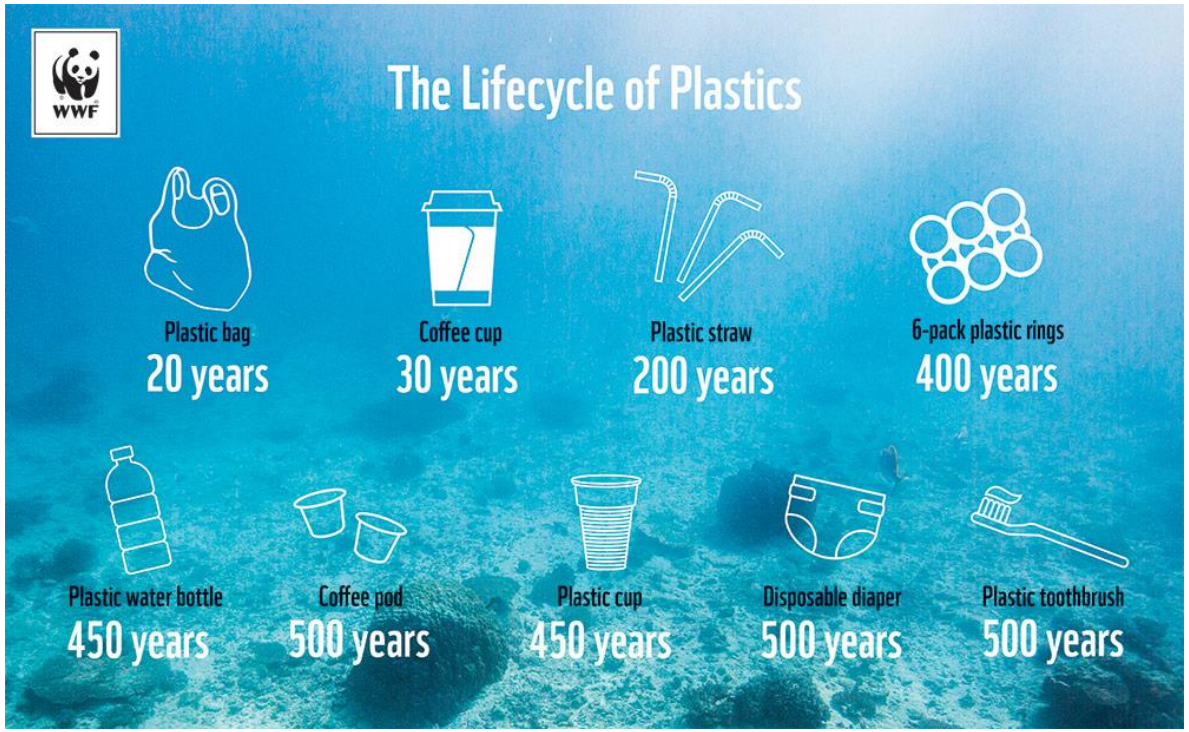
The short history of plastic

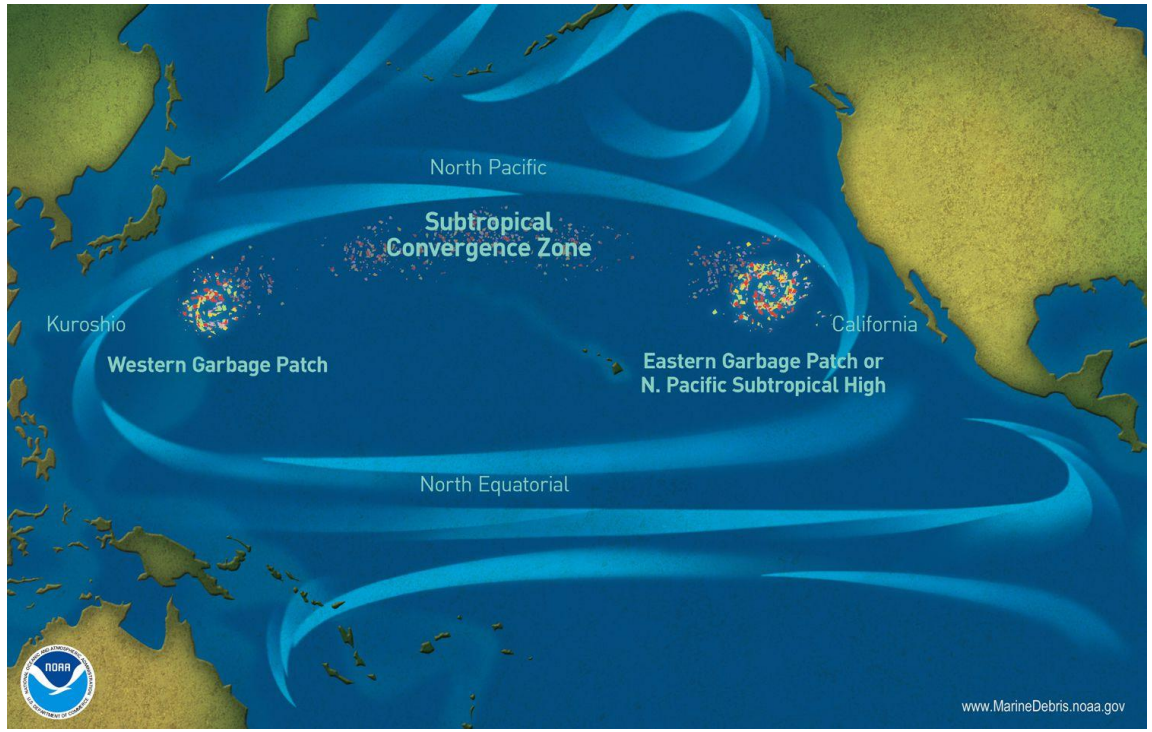
- Discovery of polystyrene (1839) and PVC (1872).
- Commercial production of PVC begins—1920s.
- 1930-1960: polyethylene, polyethylene terephthalate, polypropylene.
- 1960: plastic debris recorded in guts of seabirds.
- First concerns about uptake of chemicals from plastics by wildlife—1972.
- MARPOL restrictions on dumping of garbage from ships—1988.
- Plastic debris reported in deep sea—2000



1945 book 'Plastics' by Yarsley & Couzens: *This [imaginary] plastic man will come into a world of colour and bright shining surfaces where childish hands find nothing to break, no sharp edges, or corners to cut or graze, no crevices to harbour dirt or germs . . . . The walls of his nursery, his bath . . . Al his toys, his cot, the moulded light perambulator in which he takes the air, the teething ring he bites, the unbreakable bottle he feeds from [all plastic]. As he grows he cleans his teeth and brushes his hair with plastic brushes, clothes himself with in plastic clothes, writes his first lesson with a plastic pen and does his lessons in a book bound with plastic. The windows of his school curtained with plastic cloth entirely grease- and dirt-proof . . . and the frames, like those of his house are of moulded plastic, light and easy to open never requiring any paint.* And this plastic man lives happily until, at old age: *he/she wears a denture with silent plastic teeth and spectacles with plastic lenses . . . until at last he sinks into his grave in a hygienically enclosed plastic coffin.*

Half-life of plastic and its accumulation in the great Pacific garbage patch

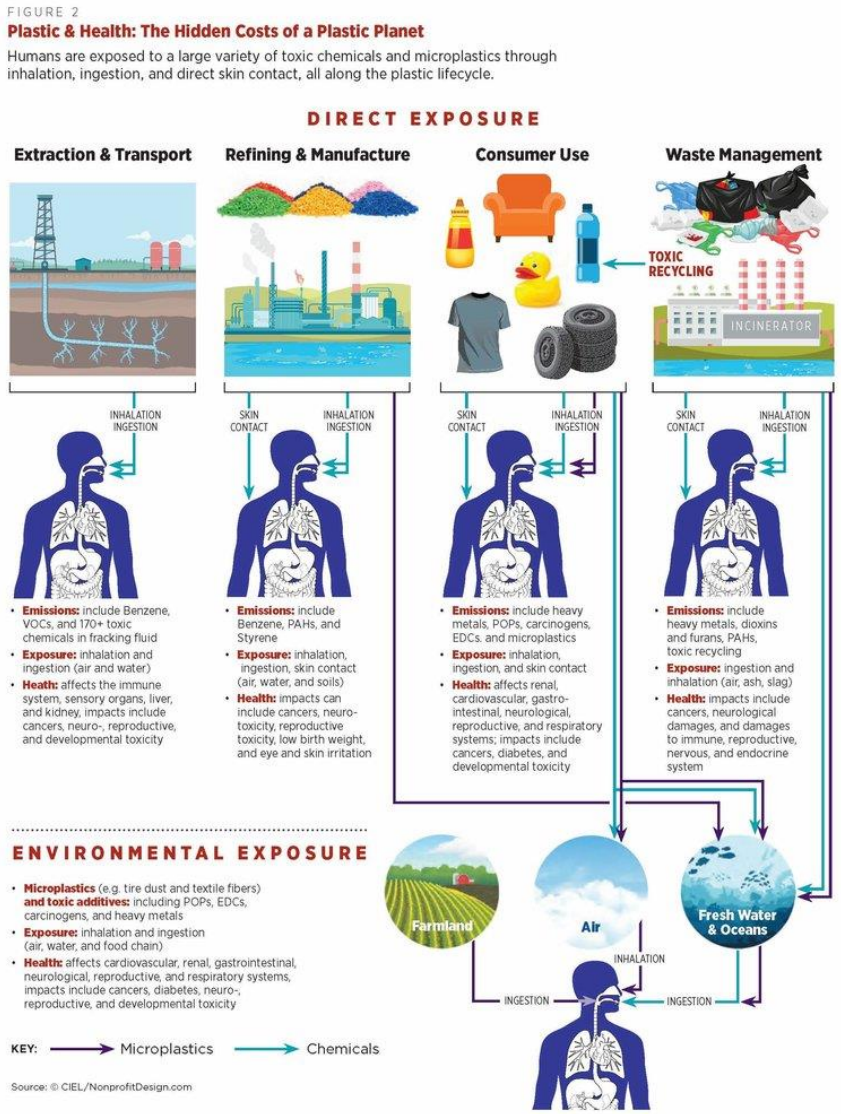




- Remarkable half-life.
- Unfortunately, often single-use.

2. Microplastic and human health: What some people claim

Plastic-derived polyamide textiles **are absorbed into the skin when worn**. Through the simple mechanical process of abrasion, each time you wear these textiles, tiny plastic fibres are rubbed off and absorbed into the biggest organ in your body - your skin



PLASTIC FREE JULY: DOES PLASTIC PUT OUR BODY AT RISK?

July 23, 2020

We all consume too much plastic. Literally. There is plastic in the food we eat, the water we drink and even the air we breathe. Unfortunately, most people don't realize that when plastic enters our body, it might make us sick. The chemicals in plastic have been linked to adverse health effects like cancer, diabetes, obesity, infertility, and neurological problems. There is enough evidence suggesting that plastic harms our health.

3. Microplastic and human health: What evidence do we have?

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B

Phil. Trans. R. Soc. B (2009) **364**, 2153–2166
doi:10.1098/rstb.2009.0053

Review

Plastics, the environment and human health: current consensus and future trends

Richard C. Thompson[1,*], Charles J. Moore[2], Frederick S. vom Saal[3] and Shanna H. Swan[4]

Plastic contamination of the food chain: A threat to human health?

R.H. Waring[a,*], R.M. Harris[a], S.C. Mitchell[b]

[a] *School of Biosciences, University of Birmingham, Birmingham, UK*
[b] *Computational and Systems Medicine, Faculty of Medicine, Imperial College, London, UK*

nature > news feature > article

NEWS FEATURE | 04 May 2021

Microplastics are everywhere – but are they harmful?

Scientists are rushing to study the tiny plastic specks that are in marine animals – and in us.

Environmental Science & Technology

Critical Review

pubs.acs.org/est

Plastic and Human Health: A Micro Issue?

Stephanie L. Wright[*,‡] and Frank J. Kelly[‡]

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B

Phil. Trans. R. Soc. B (2009) **364**, 1973–1976
doi:10.1098/rstb.2009.0054

Introduction

Our plastic age

Richard C. Thompson[1,*], Shanna H. Swan[2], Charles J. Moore[3] and Frederick S. vom Saal[4]

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B

Phil. Trans. R. Soc. B (2009) **364**, 2079–2096
doi:10.1098/rstb.2008.0281

Review

Components of plastic: experimental studies in animals and relevance for human health

Chris E. Talsness[1,*], Anderson J. M. Andrade[2], Sergio N. Kuriyama[3], Julia A. Taylor[4] and Frederick S. vom Saal[4,]

(Micro)plastic is more than just synthetic carbon polymers – plastic additives

- Phthalates
  - ‘Plasticizers’, softening of PVC.
  - DMP
  - DEP
  - DAP
  - DPP
  - …
  - …
- Bisphenol A (BPA) and other flame retardants
- Polybrominated diphenyl ethers

- Have shown potential as endocrine-disrupting compounds, with reproductive and developmental effects.
- Number of mouse and human studies limited.
- In the absence of clinical studies, very complex to assess epidemiologically, see e.g. Meeker, et al. Phil. Trans. R. Soc. B. 2009.
- Not the focus of this Journal Club.

Microplastic everywhere – but are they harmful?

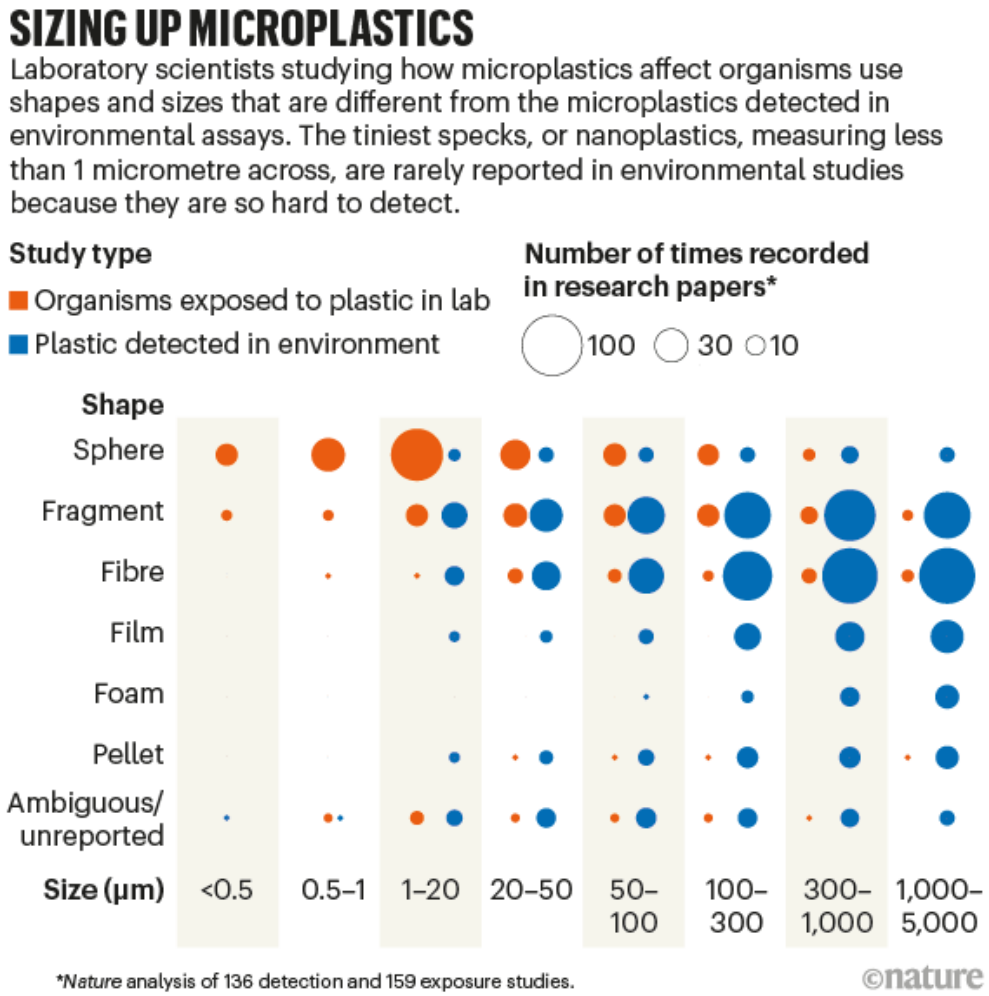
- Worry about microplastic for almost 20 years.
- Most studies have focused on **risk to marine life**.
- **Microplastic everywhere**: deep oceans, Arctic snow and ice, shellfish, table salt, drinking water, beer, air, rain.
- Tiny pieces **can take decades to degrade fully**.
- Level of **exposure** to microplastic in almost all species.
- Children and adults might **ingest from dozens to 100,000 microplastic specks each day**. Each year, plastic of about the mass of a credit card (Nor et al. Environ. Sci. Technolg. 2021).
- **Nanoplastic** (< 1 µm) are usually excluded from studies because they **can hardly be measured** unless pyroloysis-gas chromatography-mass-spectrometry is used, which is expensive.
- The larger microplastics are more likely to exert negative effects, if any, through **chemical toxicity**.
- Nanoplastic may be directly toxic.
- **Plasticizers**, **stabilizers** and **pigments** to plastics can be hazardous.
- But whether ingesting microplastics significantly raises our exposure to these chemicals depends on how quickly they move out of the plastic specks and how fast the specks travel through our bodies.
- **Factors that are entirely understudied**.

Lim, Nature News Feature, 2021

Microplastic everywhere – but are they harmful?

- Size and shape of microplastic might be important when studying effects on health.
- Marine studies have typically employed spheres but now move to more realistic conditions, including fibres and fragments.
- Zooplankton is the base of the marine food web – damage to it may be extremely impactful.

Red microplastic fibres wrap around a ***Temora*** copepod, a species of **zooplankton**. Credit: Plymouth Marine Laboratory



Lim, Nature News Feature, 2021

Microplastic everywhere – but are they harmful?

- **No direct human studies**.
- The only available studies rely on laboratory experiments that expose **cells or human tissues** to microplastics, or use animals such as mice or rats.
- Mice fed large quantities of microplastics showed inflammation in their small intestines (Li et al. Chemosphere 2020).
- Mice exposed to microplastics in two studies had **a lowered sperm count** (Jin et al. Hazard. Mater. 2021) and **fewer, smaller pups** (Park et al. Toxicol.Lett. 2020), compared with control groups.
- Most of the studies also used polystyrene spheres, which do not represent the diversity of microplastics that people ingest.
- Could microplastic remain in the human body, potentially accumulating in some tissues?

Lim, Nature News Feature, 2021

Article | Published: 19 October 2020

Microplastic release from the degradation of polypropylene feeding bottles during infant formula preparation

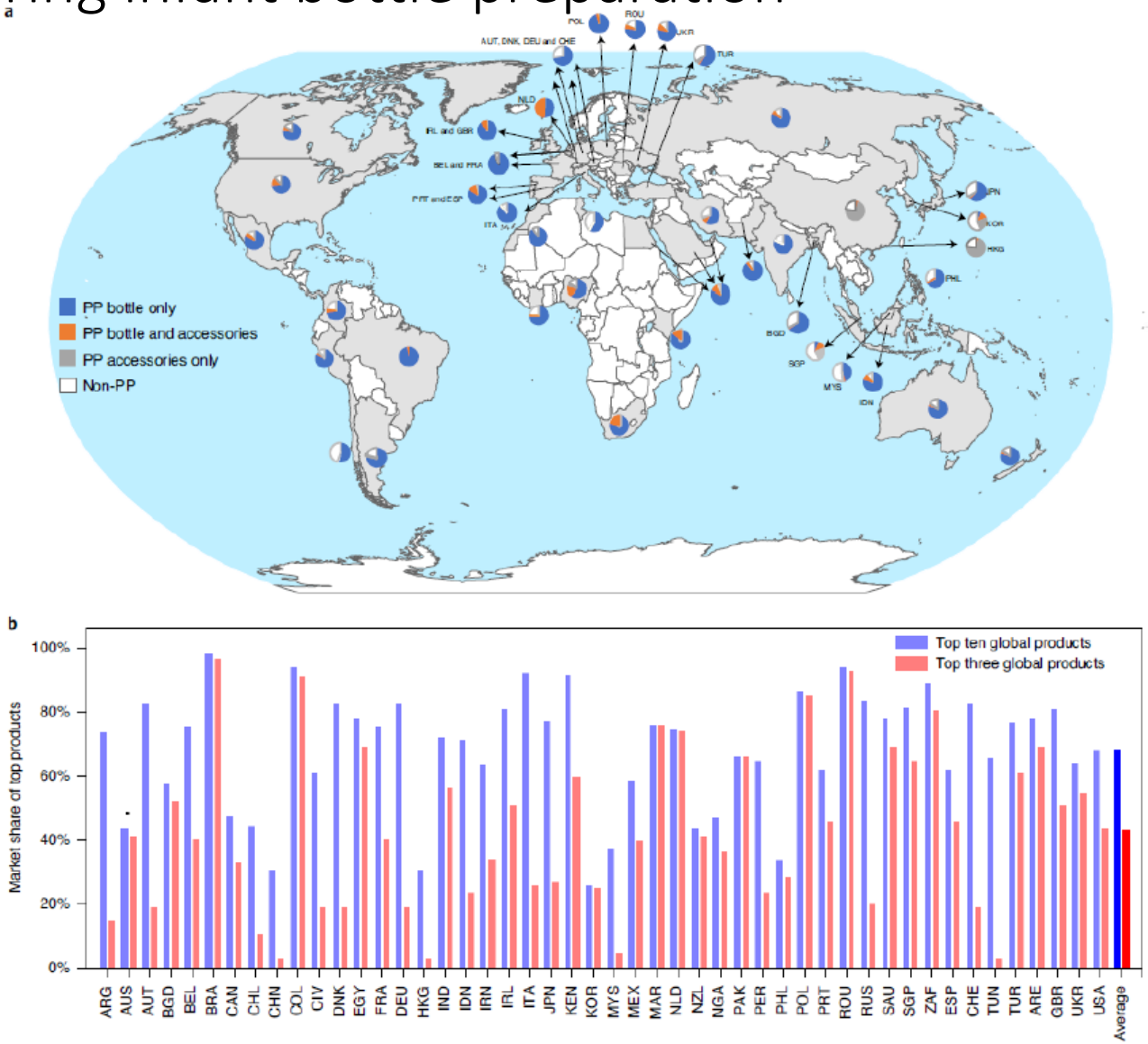
Dunzhu Li, Yunhong Shi, Luming Yang, Liwen Xiao, Daniel K. Kehoe, Yurii K. Gun'ko, John J. Boland & Jing Jing Wang

Nature Food **1**, 746–754 (2020) | Cite this article

- Microplastics (MPs) are a global concern due to their potential risk to human health.
- **Estimated MPs consumption** via food chain and inhalation pathways ranges from **74,000 to 211,000** particles annually in the US.
- MPs have been detected in human stool.
- Exposure to MPs can induce **gut microbiota dysbiosis and lipid metabolism disorder in mice**.
- Sub-micron MPs can penetrate the fish blood-brain barrier, inducing brain damage and behavioural disorders.
- Rather than focusing on water sources, **direct impact of MP to humans**.
- Polypropylene-based products are commonly used for food preparation and storage, but their **capacity to release microplastics** is poorly understood.
- Investigated the potential **exposure of infants to microplastics** from consuming formula prepared in polypropylene infant feeding bottles (**PP-IFBs**).

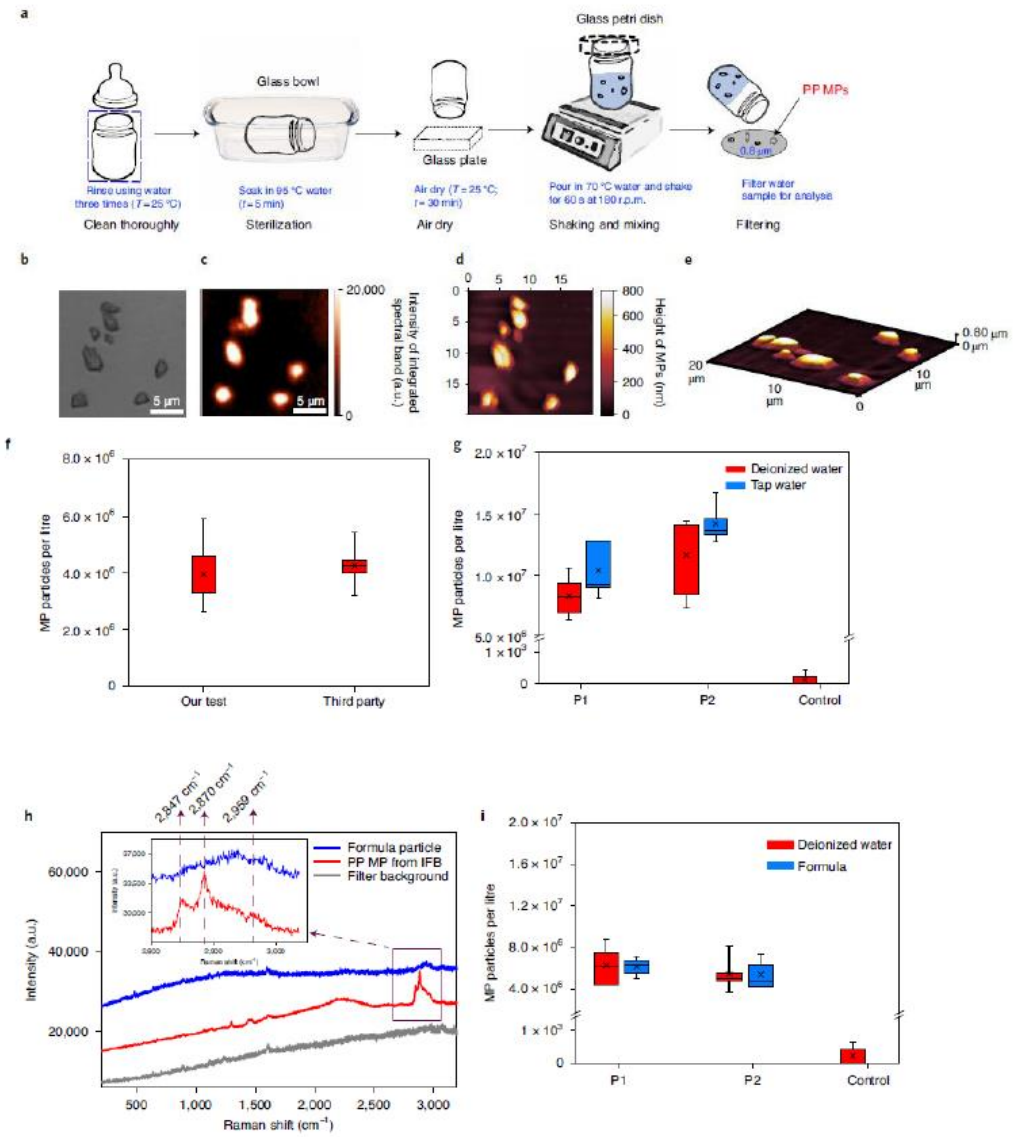
Microplastic formation during infant bottle preparation

- Infant-feeding bottles:
  - PP bottle only
  - PP bottle and accessories
  - PP accessories only
  - Non-PP
- To assess prevalence of PP-IFBs, mining of Amazon sale data using Jungle Scout platform from 48 regions.
- PP-containing products account for 82.5% of global IFB market.
- The ten most common products were used in the study.



Microplastic formation during infant bottle preparation

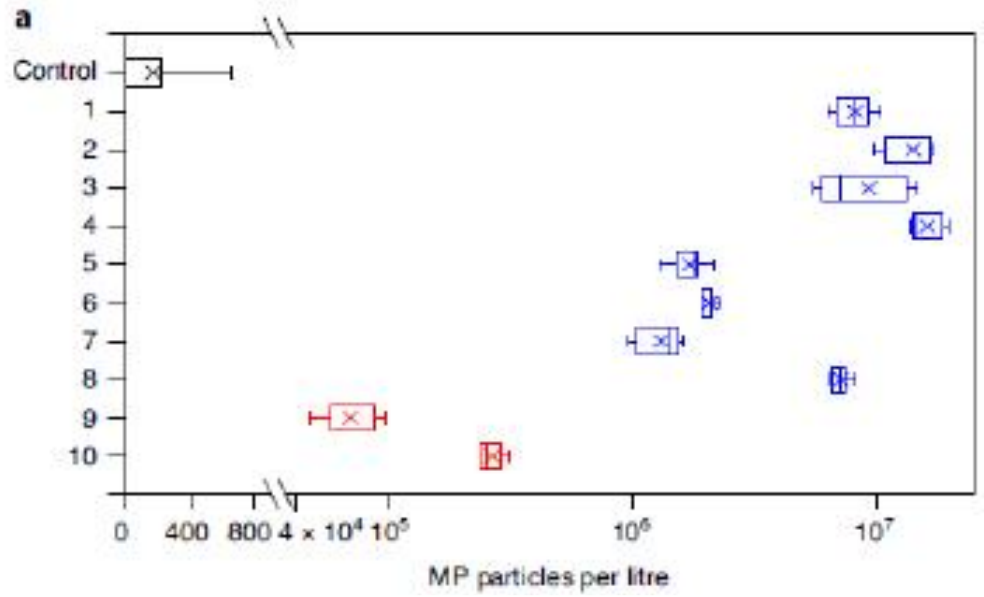
- Standard formula-preparation steps involving WHO-recommended **cleaning**, **sterilising**, and **mixing** techniques.
- **Cleaning of bottle, sterilization, air drying, formula preparation at 70 °C, filtering of water sample**.
- Filtering done using **0.8 µm gold-coated filter**.
- Quantity and topography of the PP-MPs assessed using **Raman spectroscopy** (c) and **atomic force microscopy** (d/e).
- **DI water**, **tap water or formula** does not significantly affect the MPs release from PP products (g,i).
- Measurement confirmed by third party (f).
- Usage of DI water throughout the study.

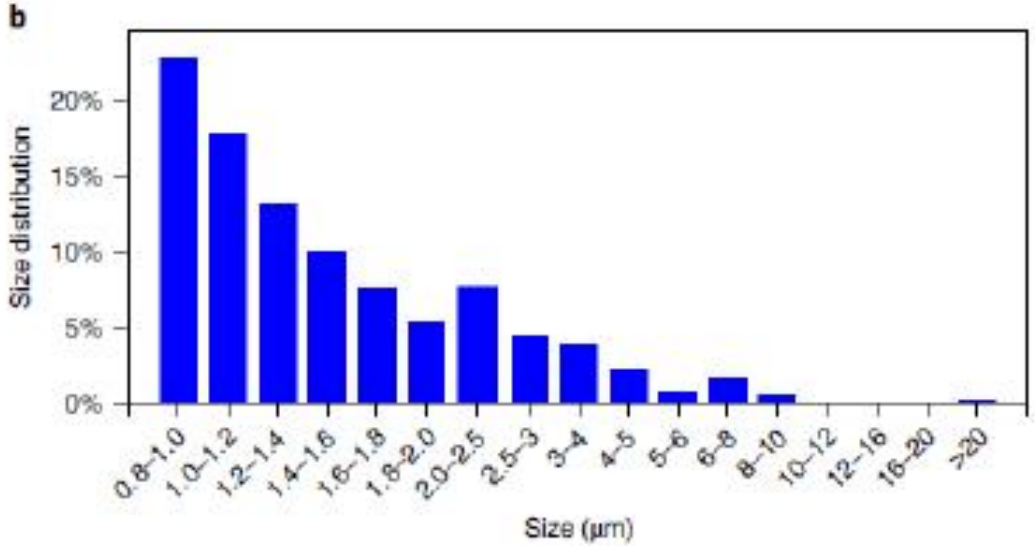


Microplastic formation during infant bottle preparation

PP bottle and PP accessories

PP accessories (gravity ball, round disk)

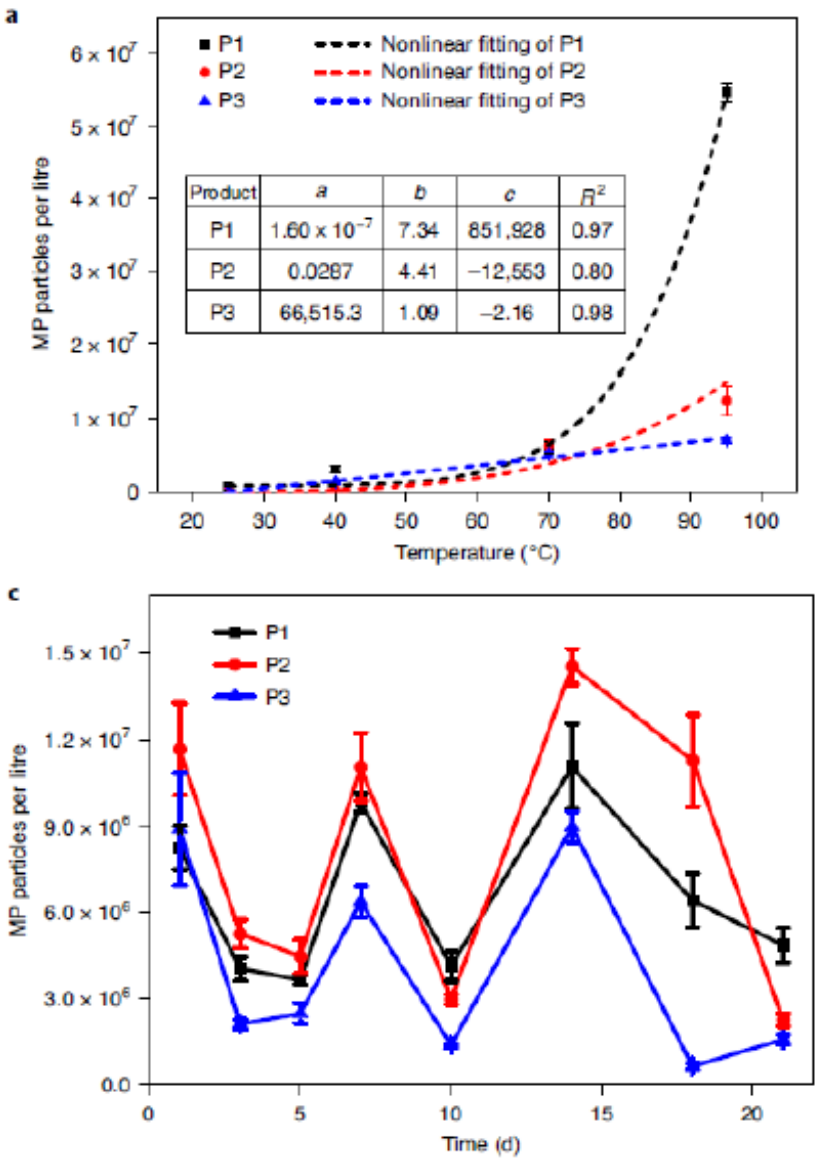




- IFB products 1-8, which have both **PP bottle bodies and PP accessories**, **released high quantities of PP-MPs**: from 1,310,000 ± 130,000 to 16,200,000 ± 1,300,000 particles/L.
- IFB products 9-10, which **only have PP accessories** (gravity ball and round disk), released 69,700 ± 9,800 and 267,000 ± 15,000 particles/L, respectively.
- Depending on the IFB product, the measured MP levels are **3 to 5 orders of magnitude higher** than the background level collected using the control sample (170 ± 54 particles/L), confirming that the PP-IFBs are the main source of measured MPs.
- Optical microscopy was used to determine the size of MPs while AFM was used to measure their surface topography and thickness. **The majority of MPs were smaller than 20 µm**.

Microplastic formation during bottle preparation

- To assess the influence of temperature on MP release, they exposed PP-IFBs to DI water with temperatures of 25 °C, 40 °C, 70 °C and 95 °C.
- Increase in propensity to shed MP with increased temperature.
- Influence of repeated usage of bottle.
- The 21-day test showed that the MPs released from all three tested products had periodic fluctuations.
- This behaviour is likely due to the multilayer structure of ordered crystalline and amorphous layers in PP.
- The gradual degradation of the ordered crystalline structure results in the exposure of amorphous regions, which are susceptible to rapid degradation.



Product	a	b	c	R^2
P1	1.60×10^{-7}	7.34	851,928	0.97
P2	0.0287	4.41	−12,553	0.80
P3	66,515.3	1.09	−2.16	0.98

SCIENTIFIC REPORTS
nature research

OPEN

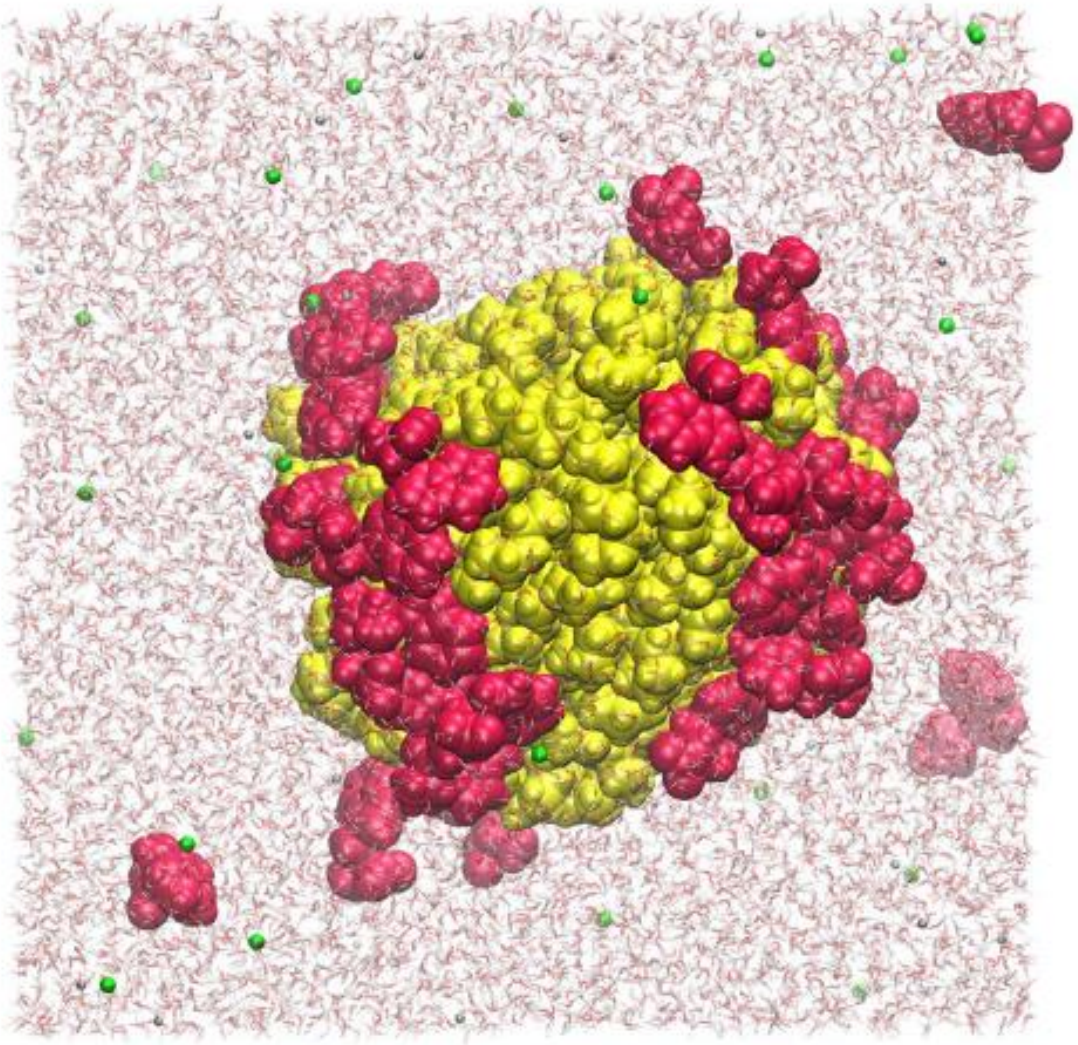
Nanoplastics can change the secondary structure of proteins

Oldamur Hollóczki* & Sascha Gehrke

- More realistic environmental risk arises from even smaller particles with sizes below 100 nm, generally called nanoplastics.
- These particles are at least **two orders of magnitude smaller than eukaryote cells**, and therefore they can potentially alter living matter on the **subcellular or molecular level**.
- Experiments showed indications that the nanoplastics have **diffused through membranes**, and have entered even the circulatory system of some mollusc organisms.
- Uncover the **interactions of nanoplastics with those biomolecules that occur within cells**, since such knowledge will aid us assessing the extent of the structural and functional damage these waste materials can cause in living organisms and in the environment.
- The sophisticated **functions** of any given protein are unambiguously defined by its characteristic **three-dimensional structure**.
- **Changes in the structure can cause defects in these functions**, which in some cases can result in the death of the cell and the organism.

Nanoplastic and protein secondary structure

- Investigation of interactions of four kinds of plastic with proteins, polyethylene (PE), polypropylene (PP), polyethylene terephthalate (PET), and nylon-6,6 (N66), all abundantly present in the environment as both micro- and nanoplastics.
- Plastic nanoparticles (PNPs) of **5 nm size**.
- Interplay of these nanoparticles with an array of **amino acids** was tested (glycine, aspartate, arginine, asparagine, phenylalanine, tryptophan).
- The amino acids with **non-polar side chains**, such as **phenylalanine** and **tryptophan**, are prone to adsorb onto the surface of the PNPs.
- This interaction is so strong, that the **PNPs collect nearly all amino acids** of this kind from the solutions.
- Forming such a **micelle-like structure** around the PNPs shows that the hydrophobic nature of nanoplastics can be masked by biomolecules, which will affect their **solubility, and their aggregation behaviour**.
- These nanoparticles are likely to directly incorporate into, and thereby interfere with the functionally crucial molecular level structure of living matter.

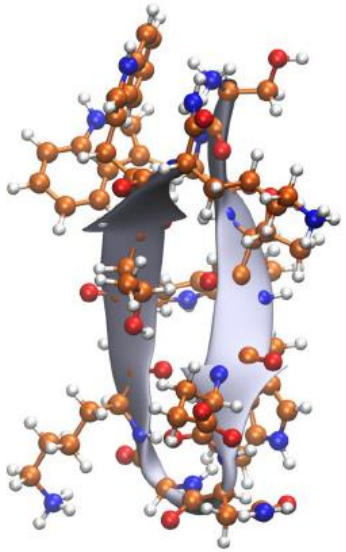


Nanoplastic and protein secondary structure

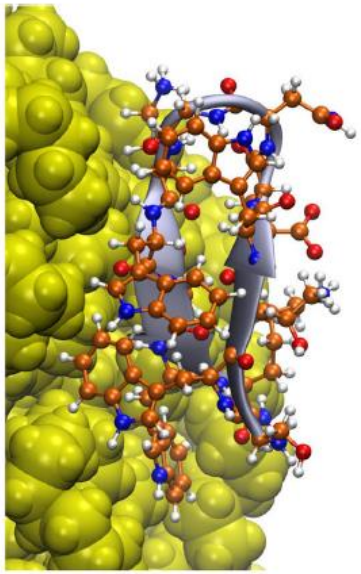
- Molecular dynamics simulations on two peptides, which represent the two most important kinds of secondary structures in proteins.
- (1) **Tryptophan zipper**, (β-hairpin structure, resembles β-sheets in proteins), (2) α-helix polypeptide of 12 alanine amino acids.
- Interaction does not induce any significant spontaneous changes in the peptide structure, as compared to that in the absence of the plastic.
- The lack of structural reorganisation, however, does not necessarily mean that the plastic has no influence on the secondary structure of the peptide, and it is conceivable that the rearrangement is kinetically hindered, and therefore too slow to observe in the time scales available for molecular dynamics simulations.
- Potential of mean force calculations (next figure).

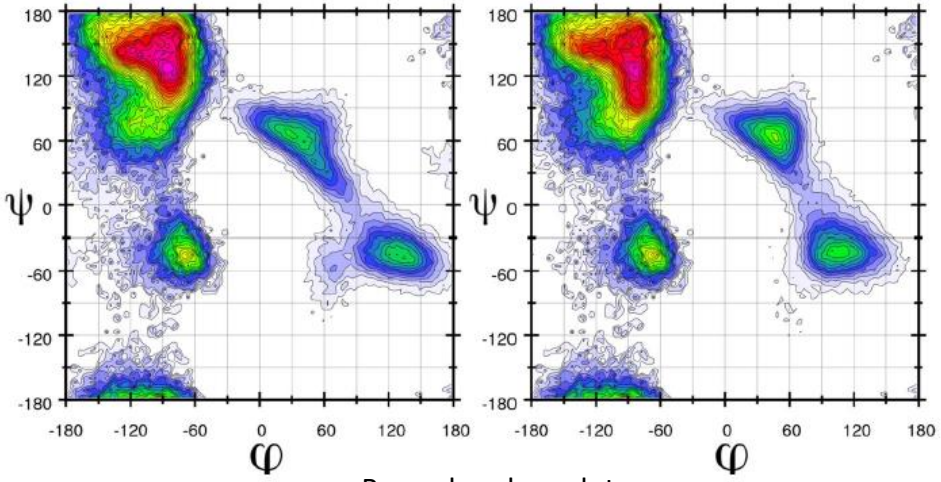
3D-Structure of tryptophane zipper

Absence of polyethylene PNPs



Presence of polyethylene PNPs

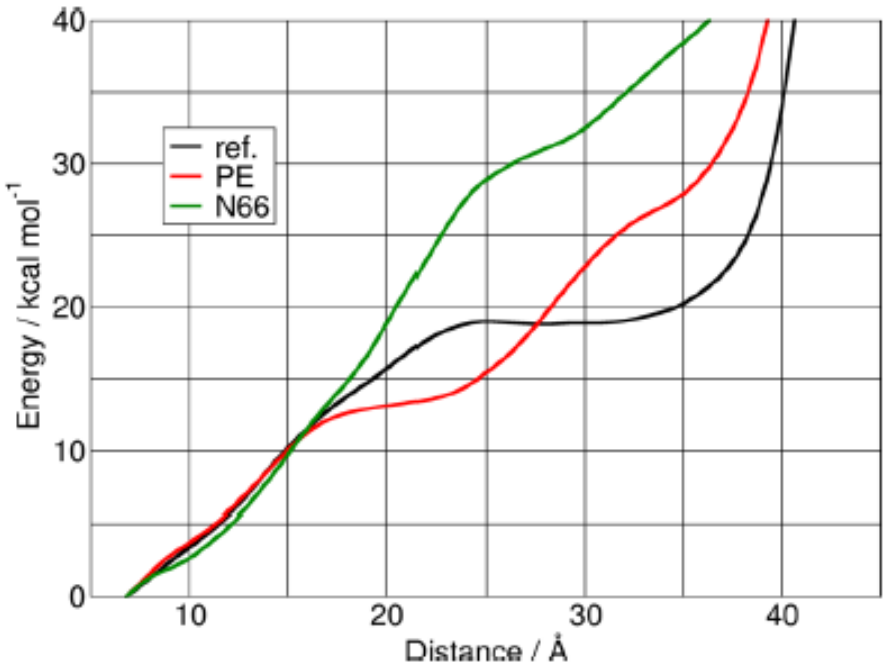




Ramachandran plot

Nanoplastic and protein secondary structure

- Characterisation of the **stability of this β-hairpin structure** through the energetics of increasing the **distance between the C-terminal carboxyl carbon atom and the N-terminal nitrogen atom** (labelled here as dC-N).
- In the absence of the PNPs the free energy constantly increases until ca. **dC-N = 25 Å**, where it levels out at **19 kcal mol−1**, which is the energy demand of breaking all the intramolecular hydrogen bonds within the peptide.
- After ca. **dC-N = 35 Å**, the free energy exhibits a steep increase, which can be attributed to the stretching of the covalent bonds of the peptide backbone after reaching a completely linear conformation.
- **The presence of the nylon nanoparticle apparently hinders the disintegration of the β-hairpin structure.**

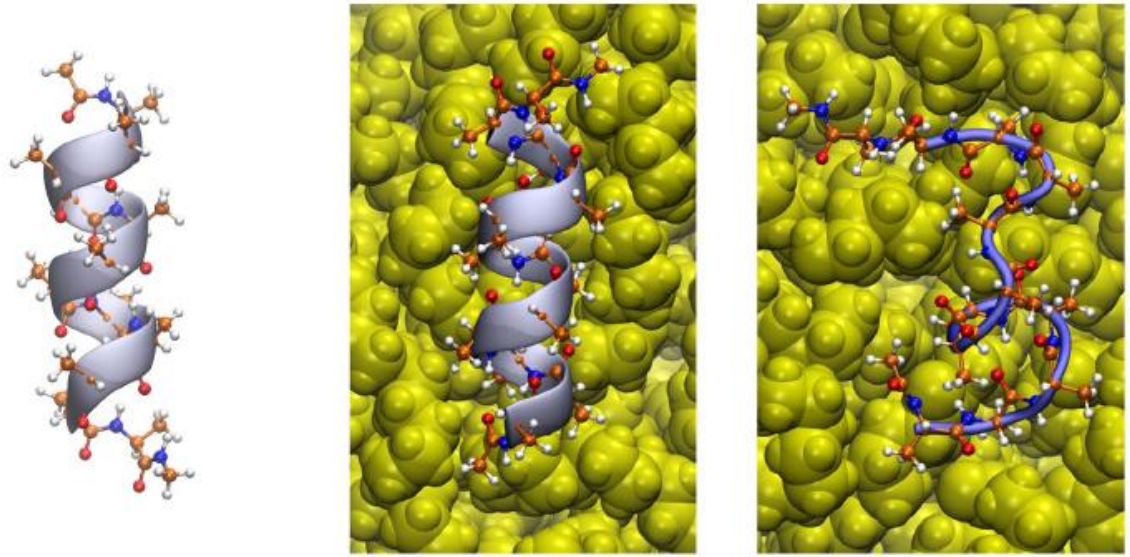


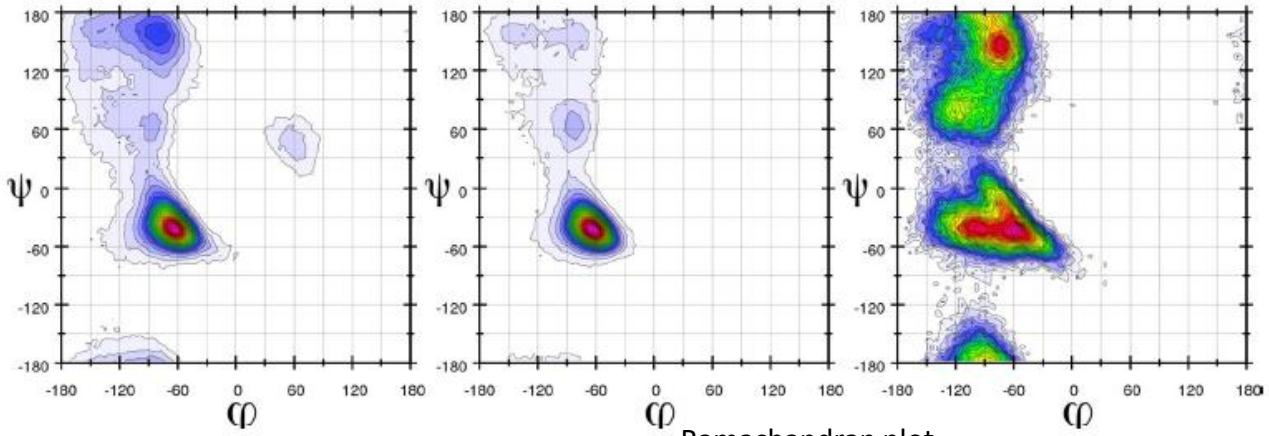
Nanoplastic and protein secondary structure

- By hindering the mobility of the two terminal amino acids, the helical structure is even stabilized further.
- On the **nylon particle, however, severe changes in the α-helix can be observed**.
- Under closer scrutiny, the helical backbone of the peptide appears to have **changed spontaneously into a β-loop-like structure**.
- Nylon: **presence of amide moieties** on its surface.
- These groups offer a **set of hydrogen bond donor and acceptor sites** at the surface to proteins, which are expectedly similar in strength to the intramolecular protein-protein hydrogen bonds.
- **Strong competition to those hydrogen bonds**, which are necessary for the integrity of the helical structure, and thereby define the secondary structure of the peptide.
- ***The plastic forms a template for the peptide, to which it is forced to adjust its own structure.***

3D-Structure of alpha helix

Absence of PNPs | Presence of polyethylene PNPs | Presence of nylon-6,6 PNPs





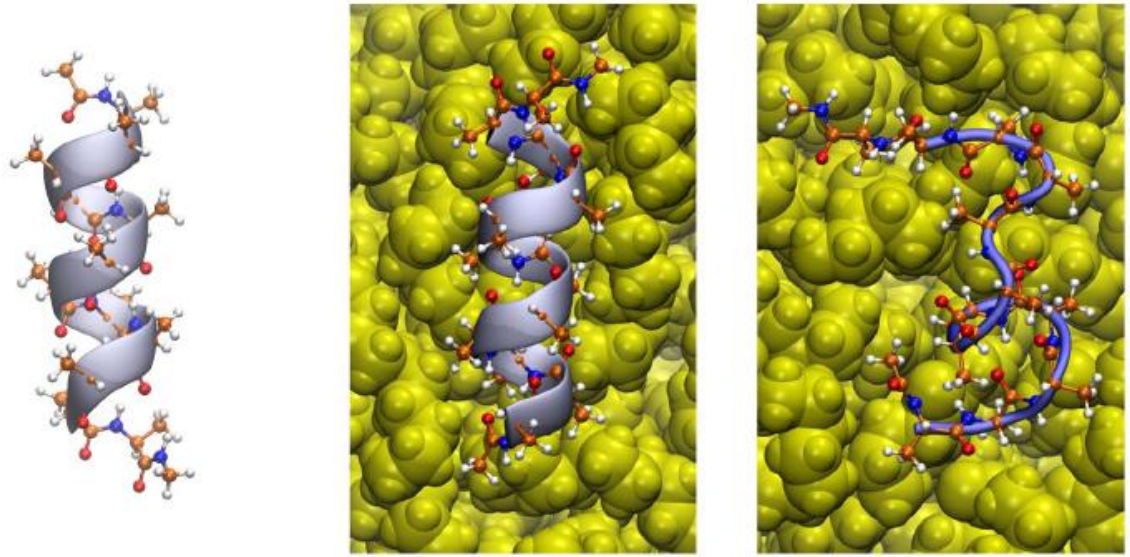
Ramachandran plot

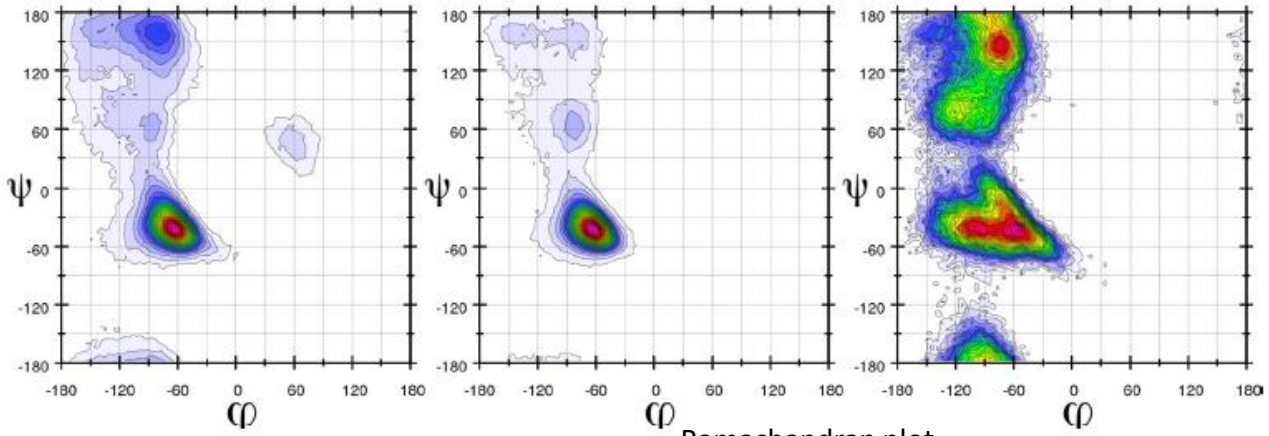
Nanoplastic and protein secondary structure

- By hindering the mobility of the two terminal amino acids, the helical structure is even stabilized further.
- On the **nylon particle, however, severe changes in the α-helix can be observed**.
- Under closer scrutiny, the helical backbone of the peptide appears to have **changed spontaneously into a β-loop-like structure**.
- Nylon: **presence of amide moieties** on its surface.
- These groups offer a **set of hydrogen bond donor and acceptor sites** at the surface to proteins, which are expectedly similar in strength to the intramolecular protein-protein hydrogen bonds.
- **Strong competition to those hydrogen bonds**, which are necessary for the integrity of the helical structure, and thereby define the secondary structure of the peptide.
- ***The plastic forms a template for the peptide, to which it is forced to adjust its own structure.***

3D-Structure of alpha helix

Absence of PNPs | Presence of polyethylene PNPs | Presence of nylon-6,6 PNPs





Ramachandran plot

Prüst *et al. Particle and Fibre Toxicology* (2020) 17:24
https://doi.org/10.1186/s12989-020-00358-y

Particle and Fibre Toxicology

REVIEW **Open Access**

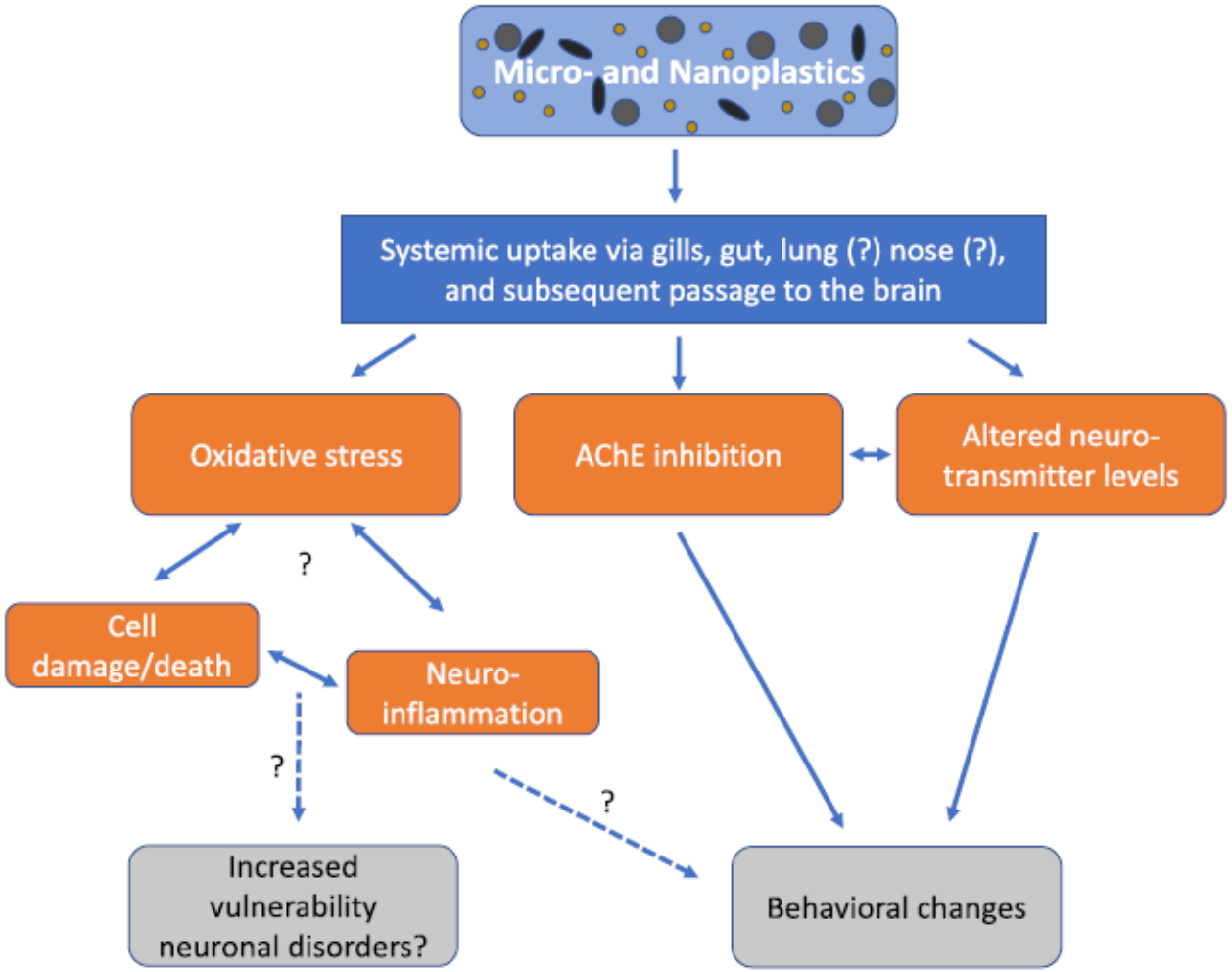
The plastic brain: neurotoxicity of micro- and nanoplastics

Minne Prüst, Jonelle Meijer and Remco H. S. Westerink*

- Marine bulk plastics are subject to fragmentation through photodegradation and erosion by wave action, contact with animals, abrasion with sand and by the water itself.
- Secondary microplastics (defined as particles with a diameter 0.1 µm to 5 mm) and secondary nanoplastics (defined as particles with a diameter below 100 nm).
- Primary micro- and nanoplastics are deliberately produced in ultra-small sizes to serve as components in cosmetics, paints, personal care products or fabrics.
- Humans are exposed to micro- and nanoplastics via consumption of contaminated (marine) animals and other food and consumer products such as toothpaste, beer, honey, salt and sugar.
- **Uptake** of micro- and nanoplastics (≤0.3 µm) and **subsequent translocation to the liver**, **spleen** and **lymphatic systems of rodents** has been reported decades ago.
- In humans, microsized plastic fibers have been **detected in lung tissue**, indicating possible translocation of micro- and nanoplastics into the human body via particle inhalation and limited gastrointestinal uptake of biodegradable polymeric microparticles has been reported.
- The potential health risks resulting from micro-and nanoplastics exposure, uptake and translocation is poorly investigated and is an important matter of ongoing debate.

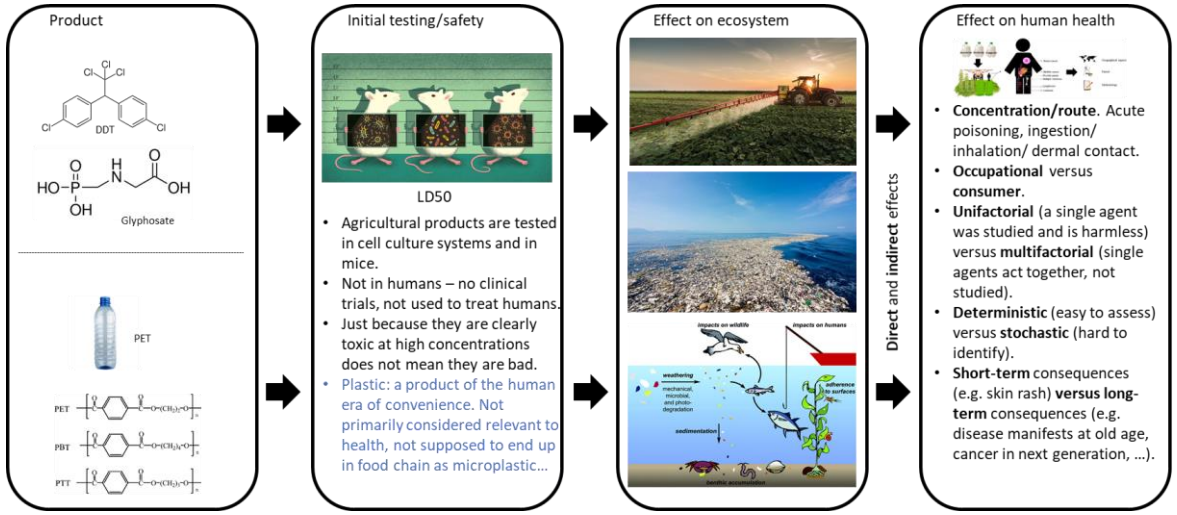
Neurotoxicity of micro- and nanoplastics

- Plastic particles can reach the systemic circulation and ultimately the brain via uptake through the gills, gut and possibly also the lungs or directly via the nasal cavity.
- Once in the brain, micro- and nanoplastics **can induce oxidative stress**, potentially resulting in cellular damage and neuroinflammation, which may ultimately increase onset and development of neurodevelopmental and/or neurodegenerative disorders.
- Micro- and nanoplastics in the brain **can also result in inhibition of AChE** and **changes in neurotransmitter levels**, which likely contribute to the observed behavioral changes.
- It should be noted though that most **evidence is fragmentary** and obtained from different, mainly aquatic species, highlighting the need for extensive systematic research to fully elucidate the neurotoxic potential of micro- and nanoplastics.



Conclusions I

- To date, the impact of nano-/microplastic, if any, to human health is unclear.
- This is because tiny plastic fragments are heavily understudied in animal models as well as in humans.
- The ease at which many of us handle plastic – including its entirely unknown long-term consequences to human health – is surprising (even more so when the administration of an mRNA particle into muscle, post multiple clinical studies, may lead to endless public discussions).



- For both pesticides as well as microplastics, the **absence of well-controlled studies** complicates the assessment tremendously.

Conclusions II

- 25 trillion macro & 51 trillion microplastics litter the oceans.
- Only 1% of marine litter floats, everything else sinks to the sea floor.
- With or without drastic direct effects on human health, it seems sensible to move towards a more sustainable way of living.

PLASTIC POLLUTION

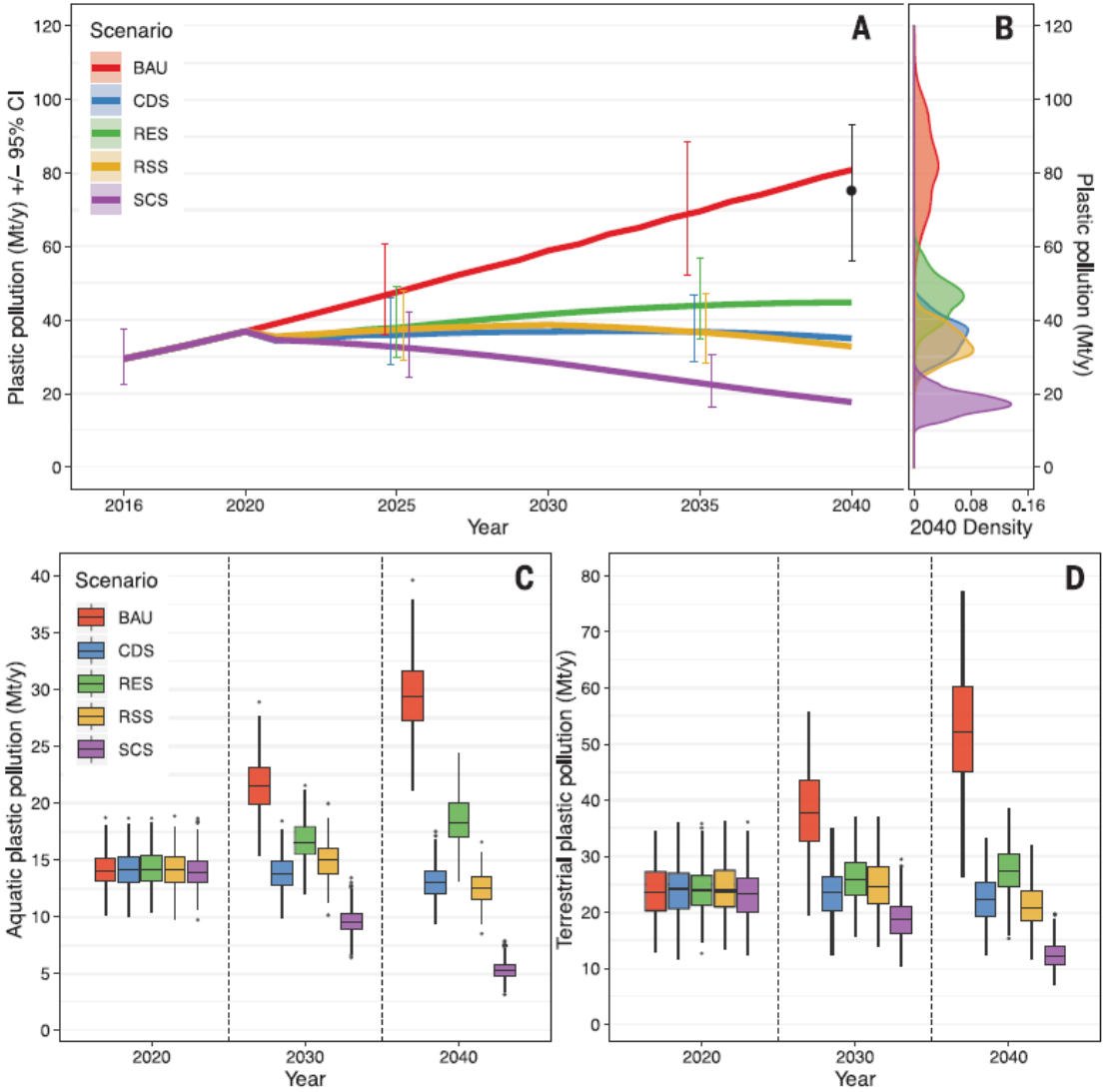
Evaluating scenarios toward zero plastic pollution

Winnie W. Y. Lau[1*†], Yonathan Shiran[2*†], Richard M. Bailey[3*†], Ed Cook[4], Martin R. Stuchtey[2,5], Julia Koskella[2], Costas A. Velis[4*], Linda Godfrey[6], Julien Boucher[7,8], Margaret B. Murphy[1], Richard C. Thompson[9], Emilia Jankowska[2], Arturo Castillo Castillo[10], Toby D. Pilditch[3], Ben Dixon[2], Laura Koerselman[2], Edward Kosior[11], Enzo Favoino[12], Jutta Gutberlet[13], Sarah Baulch[1], Meera E. Atreya[2], David Fischer[2], Kevin K. He[1], Milan M. Petit[2], U. Rashid Sumaila[14], Emily Neil[3], Mark V. Bernhofen[4], Keith Lawrence[1], James E. Palardy[1*†]

- Plastic pollution is globally ubiquitous. It is found throughout the oceans, in lakes and rivers, in soils and sediments, in the atmosphere, and in animal biomass. This proliferation has been driven by **rapid growth in plastic production and use** combined with **linear economic models that ignore the externalities of waste**.
- A sharp rise in single-use plastic consumption and an expanding “throw-away” culture have exacerbated the problem.
- Range of detrimental effects of plastic pollution.
  - Nearly 700 marine species and more than 50 freshwater species are known to have ingested or become entangled in macroplastic, and there is growing evidence that plastic is ingested by a wide range of terrestrial organisms.
  - Microplastics are also increasingly found in the human food system, although their impacts on human health are difficult to assert and require further research.
  - Plastic production, collection, and disposal are also major sources of greenhouse gas (GHG) emissions.
  - Plastic pollution affects many aspects of human well-being: affecting the aesthetics of beaches, blocking drainage and wastewater engineering systems, and providing a breeding ground for disease vectors.
- Variety of solutions to the plastic pollution problem have been proposed at local, national, and regional levels.
  - Postconsumption management.
  - Reducing plastic through replacement with alternative products.
  - Bans or levies on select plastic products.
  - The scientific community and nongovernmental organizations are also working to identify solutions.
- Global evidence-based strategy that includes practical and measurable interventions aimed at reducing plastic pollution does not yet exist.

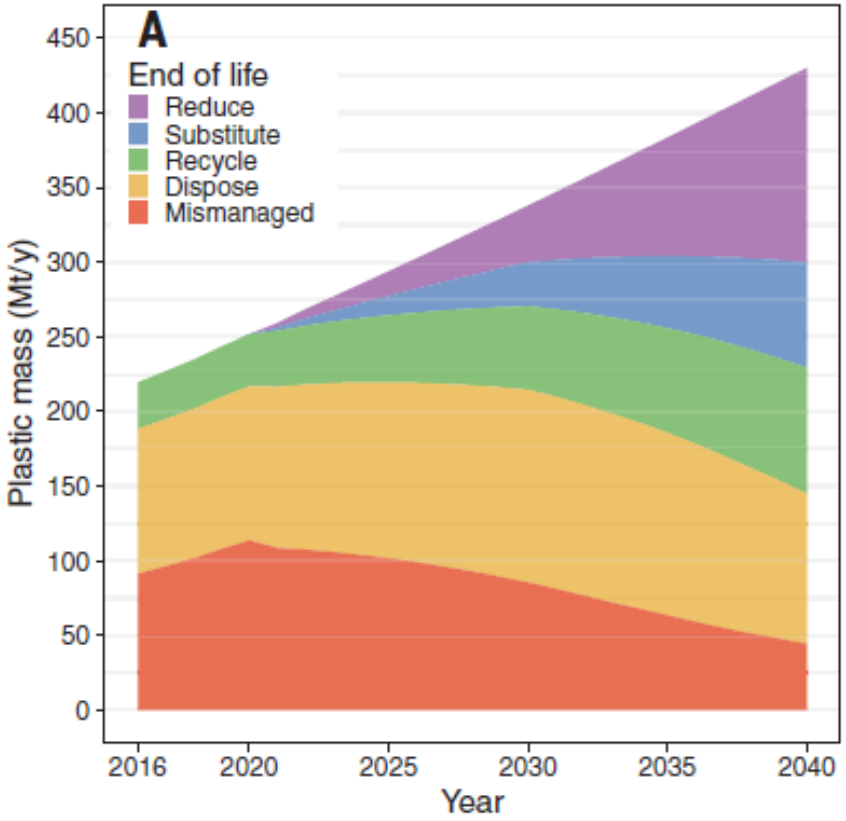
Scenarios towards zero plastic pollution

- Designing an effective global strategy requires an understanding of the mitigation potential of different solutions and the magnitude of global effort needed to appreciably reduce plastic pollution.
- Modelling of stocks and flows of municipal solid waste and four sources of microplastics through the global plastic system for five scenarios between 2016 and 2040:
  - Business as Usual (BAU)
  - Collect and Dispose (CDS)
  - Recycling (RES)
  - Reduce and Substitute (RSS)
  - System Change (SCS)
- Many model inputs have a high degree of uncertainty, which was propagated with Monte Carlo sampling.
- Annual rates of plastic pollution entering the environment estimated from 300 Monte Carlo simulations.
  - (A) Time series of plastic pollution entering aquatic and terrestrial ecosystems, in million metric tons per year, with Kernel density estimates (B).
  - (C) aquatic and (D) terrestrial plastic pollution. Approximately 3 fold increase in pollution in the BAU approach.
  - If the current commitments to reducing plastic pollution assuming full implementation are realized, only minor reduction of plastic pollution by 2040.
  - Although there is an effect, it is clearly not enough.

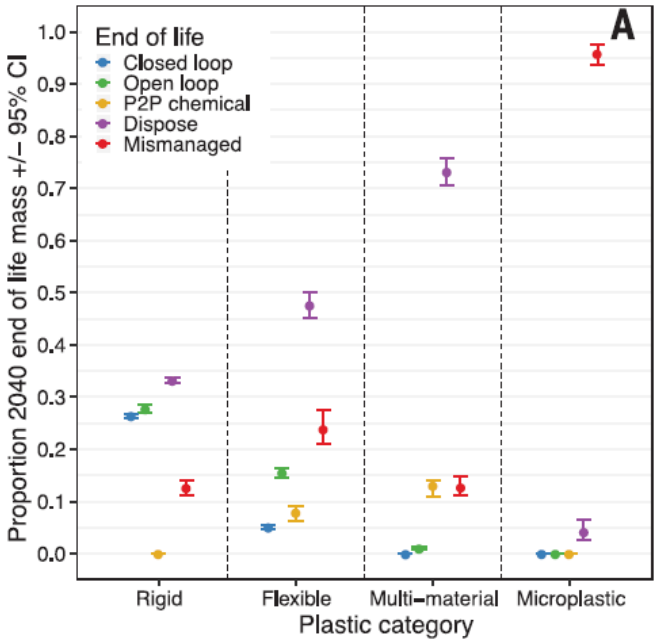


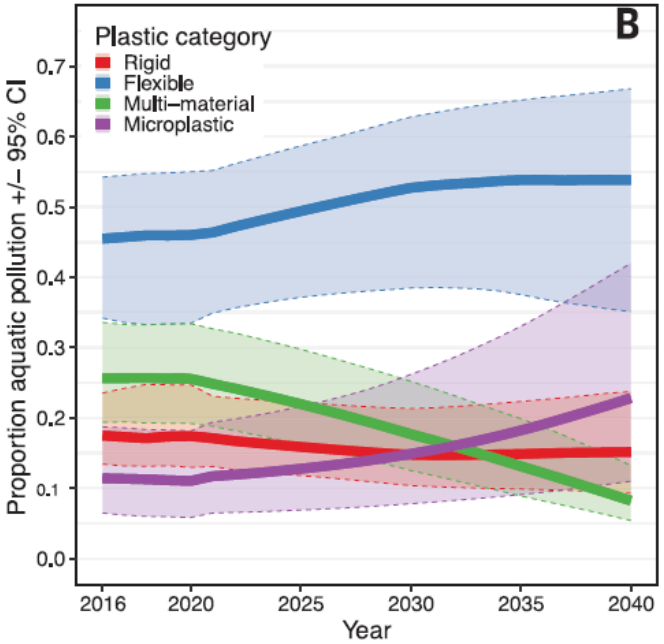
Scenarios towards zero plastic pollution

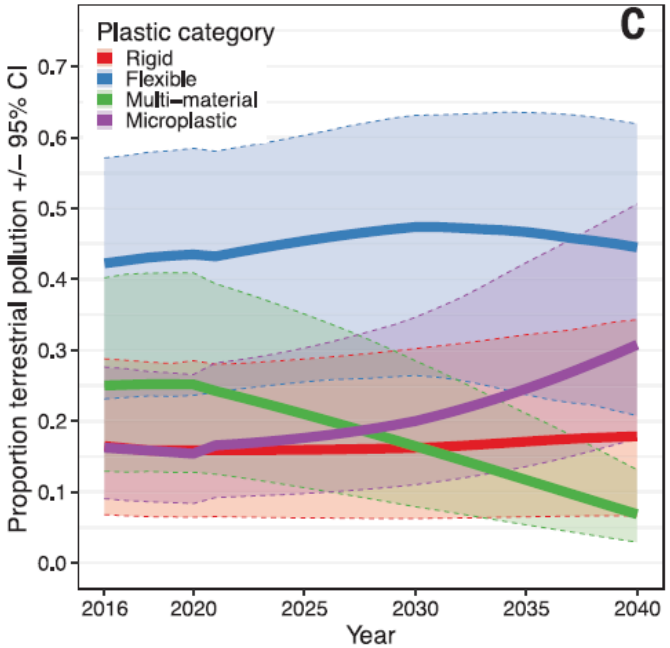
- For the best scenario, the system change scenario, they look at end-of-life fates of municipal waste plastic.
- Plastic waste coming from
  - mismanagement and disposal is decreased
  - recycling, substitution, and reduction is increased.
- Taken together, the System Change scenario moves toward achieving a circular economy in which resources are conserved, waste generation is minimized and GHG emissions reduced.



Scenarios towards zero plastic pollution







- Fate of plastic MCW by plastic type under the **System Change Scenario** (SCS).
- Recycling solutions: closed loop, open loop, p2p chemical. No recycling: dispose, mismanaged.
- (A) For most materials but not for microplastic, recycling solutions could be found by 2040 but for all plastic types, disposal of plastic is still predominating.
- (B) and (C): Proportion of plastic type entering aquatic and terrestrial systems.

Scenarios towards zero plastic pollution

- **These analyses indicate that urgent and coordinated action combining pre- and postconsumption solutions could reverse the increasing trend of environmental plastic pollution**.
- Although no silver bullet exists, **78% of the plastic pollution problem can be solved by 2040** through the use of current knowledge and technologies and at a lower net cost for waste management systems compared with that of BAU.
- However, with long degradation times, even a 78% reduction from BAU pollution rates results in a massive accumulation of plastic waste in the environment.
- Moreover, even if this system change is achieved, plastic production and unsound waste management activities will continue to emit large quantities of GHGs.
- Further innovation in **resource-efficient and low-emission business models**, **reuse and refill systems**, **sustainable substitute materials**, **waste management technologies**, and **effective government policies** are needed.
- It is crucial to resolve the ecological, social, and economic problems of plastic pollution and achieve near-zero input of plastics into the environment.

THANK YOU