Biomaterials Science Can Offer a Valuable Second Opinion on Nature's Plastic Malady

Bryan D. James[a, *], Mark E. Hahn[b], Christopher M. Reddy[a]

[a] Department of Marine Chemistry and Geochemistry, Woods Hole Oceanographic Institution, Woods Hole, MA, USA 02543

[b] Department of Biology, Woods Hole Oceanographic Institution, Woods Hole, MA, USA, 02543

* Corresponding author

Keywords: *Wastes, Plastics, Environmental pollution, Materials, Biocompatibility, Biomedical*

Microplastics are an emerging pollutant with many fundamental questions still left unresolved. Are they toxic? How do they change over time? How long do they persist? Environmental scientists are asking many of these questions about the fate and effects of plastics in the natural environment, while biomaterials scientists have been asking the same questions for years in another environment: the human body.

The field of biomaterials encompasses all materials used in biomedical devices and therapies. (Biomaterials are not to be confused with bio-materials or biological materials, which are largely considered a class of materials with some natural origin.) Prior to the 1960s, the field of biomaterials relied on commercial plastics. Classic examples include the precursors of modern-day contact lenses and vascular grafts.[1]

Originally, there was an overly simplistic view of the interaction between biological systems and materials. Early contact lenses were made of polymethylmethacrylate (PMMA; a.k.a.

Plexiglas®) because the material met the requirements for mass production, optical clarity, machinability, etc. However, hard contact lenses also irritated patient's eyes because they lacked hydration and oxygen permeability.[2] In a comparable manner, expanded PTFE (ePTFE; a.k.a. Goretex®) or woven polyethylene terephthalate (PET; a.k.a. Dacron®) were used to make vascular grafts. Despite their non-stick characteristics in other domains, in the body they promote clotting because they did not have good hemocompatibility on their own. Today, enhancements such as modifying the surface with anticoagulant/antithrombotic agents have been used, but issues related to unwanted clotting persist for small diameter grafts.[3] Slowly, it has been recognized that there is more to consider than just the chemical and physical properties of a material. In these two examples, it became clear that the biological properties—the host response and cell-material interactions—are also important. Engineered plastics were used in new environments for which they were not designed and in which they had never been tested. Biomaterial scientists and engineers soon learned an important lesson: biology matters.

The same can be said about plastic pollution. The processes impacting the persistence and toxicity of plastics depend on where they reside. One example of this concerns the biodegradability of polylactic acid (PLA). In industrial composting conditions, PLA has a relatively short lifetime (months), but in the soil or the ocean it can persist significantly longer (years).[4] This gives us the environmental scientist's corollary to the above rule: the environment matters.

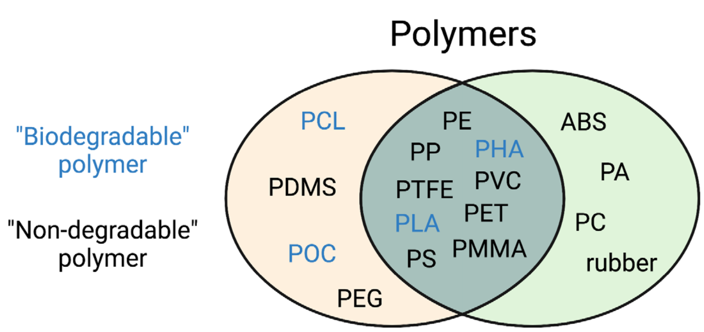
In the field of biomaterials, the issues described above catalyzed the concept of *biocompatibility*. In its most basic terms, biocompatibility is "the ability of a material to perform with an appropriate host response in a specific application".[5] It couples material to application. PMMA as a contact lens material did not give an "appropriate host response" because it caused irritated, dry eyes. New materials were investigated and developed; now, contact lenses are soft and made from hydrogel silicones or from poly(2-hydroxyethyl methacrylate) (pHEMA).[2] These biomaterials support hydration and oxygen diffusion to the underlying eye tissue, which greatly improve patient comfort. Next-generation vascular grafts look to use more hemocompatible materials such as biodegradable poly(diol citrate) elastomers (POC).[3,6] Both of these changes relied on new biomaterials.

Biomaterials science as a field progressed once it became accepted wisdom that materials should be designed from the ground up with the body and human health in mind. To do this required greater mechanistic studies of human physiology and its interaction with materials.[1] Environmental scientists are starting to do the same type of basic research to uncover the interactions between plastics and nature. A prime example has been revisiting the environmental lifetimes of plastic.[7] Once thought to be thousands of years, it is now understood to be more likely hundreds of years, exemplified by fundamental research on the photodegradation of polystyrene.[8] Biomaterials science can offer environmental science a "second opinion" on plastic pollution because the plastics of interest for both fields greatly overlap (**Figure 1**) and so offer the potential for insight from both fields to be applied to questions regarding the use of a particular plastic in either context. Already it has been suggested that organ-on-a-chip models can be used for evaluating environmental nanoparticle toxicity and that the body's response to polymeric wear particles from prostheses can inform our understanding of the body's response to microplastics.[9–11] Still, there is more room for exchange.

The most common industrial plastics have been or are of interest to both fields and the environmental conditions that plastics are subjected to in the body and in nature are very similar. Both environments are aqueous, consist of a collection of biomacromolecules, salts, and small molecules, and are biologically active. The major exception is that the environment often includes photochemical processes, where the body does not. However, the reactive oxygen species generated by sunlight in nature are similarly present in the body and are used by cells to attack pathogens and foreign materials.[1,8]

Another crossover is in the release and absorption of small molecules. The processes governing this are the same in the body and the environment and simply differ by a matter of perspective: One plastic's leachate is another plastic's released drug.[12] The collection of biomacromolecules that adsorb to plastics has been dubbed its eco-corona;[13] the same phenomenon also occurs on the surfaces of biomaterials in the form of a "bio-corona," notably by serum proteins.[14]

Of interest to environmental health scientists is the potential for microplastics to act as vectors of disease-causing microbes.[15] In principle, the interactions investigated by biomaterial scientists in terms of microbiome-material interactions and biofilm-material interactions should aid in this effort.[1,15,16]



	Biomedical	Environmental
Environment	Aqueous, ionic	Aqueous, ionic
Redox	Bio-oxidative	Photo-oxidative
Small Molecules	Released drugs	Leachates
Adsorption	Bio-corona	Eco-corona
Microbial	Microbiome, biofilms	Biofilms

Figure 1. A comparison of common polymers used and investigated in the biomedical and environmental sciences. Notably, the plastics most abundantly found in nature (PE, PP, PS, PET,

PVC) are shared between the two fields.[1,17] Additionally, many of the properties and processes of interest are the same and simply differ only on the basis of favorability e.g., in the biomedical field the release of small molecules can be favorable for drug delivery while in the environmental field the release of small molecules can be unfavorable in the form of leachates. Created with BioRender.com.

Much like in biomaterials science, environmental science would benefit from defining a term parallel to *biocompatibility* to describe the interaction of materials in the environment. In that sense, the *ecocompatibility* of a material can be thought of as the ability of a material to not disrupt the healthy functioning of the natural environment in which it exists. Pairing material and environmental context can provide a framework that is aligned with the concepts of green chemistry for both understanding and designing a material with the natural environment in mind and to recognize that the same plastic may behave differently in different environments. The framework can come full circle when considering the toxicity of environmentally derived microplastics in the body as their presence transitions from being an issue of ecocompatibility to one of biocompatibility. It should be noted that the plastics being investigated as biodegradable or eco-friendly have been used in the body for the past few decades.[1] This exchange can be a bridge for biomaterials scientists, environmental scientists, and polymer scientists to start interacting more with one another.

It stands to reason that the interests and concerns of environmental science for plastic pollution align with those held by biomaterials science. Thus, there is much to share between the two fields to tackle the challenges of plastic pollution in the environment and its impact on wildlife and human health. It would be wise for researchers investigating plastics in the environment to communicate with their peers investigating plastics in the body and vice-versa. In medicine, one doctor's opinion is good, but two are better.

ASSOCIATED CONTENT

AUTHOR INFORMATION

Corresponding Author

Bryan D. James – *Department of Marine Chemistry and Geochemistry, Woods Hole Oceanographic Institution, Woods Hole, MA, USA 02543 ORCID ID: orcid.org/0000-0002-6104-8310*

Authors

Mark E. Hahn – *Department of Biology, Woods Hole Oceanographic Institution, Woods Hole MA, USA 02543 ORCID ID: orcid.org/0000-0003-4358-2082*

Christopher M. Reddy – *Department of Marine Chemistry and Geochemistry, Woods Hole Oceanographic Institution, Woods Hole, MA, USA 02543 ORCID ID: orcid.org/0000-0002-7814-2071*

Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Financial support

Preparation of this commentary was supported by the Postdoctoral Scholar Program at the Woods Hole Oceanographic Institution, with funding provided by the Weston Howland Jr. Postdoctoral Scholarship (BDJ); the Gerstner Family Foundation (MEH and CMR); the March Marine Initiative, a program of March Limited, Bermuda (MEH); and Woods Hole Sea Grant (MEH).

Notes

The authors declare no competing financial interest.

ACKNOWLEDGEMENT

We thank Ken Kostel (WHOI) for valued discussion of the manuscript.

ABBREVIATIONS

ePTFE, expanded polytetrafluorethylene; pHEMA, poly(2-hydroxyethyl methacrylate); PA, polyamide; PEG, polyethylene glycol; PCL, polycaprolactone; PDMS, polydimethylsiloxane; POC, polycitrates; PE, polyethylene; PP, polypropylene; PHA, polyhydroxyalkanoates; PTFE, polytetrafluoroethylene; PVC, polyvinylchloride; PLA, polylactic acid; PET, polyethylene terephthalate; PS, polystyrene; PMMA, polymethylmethacrylate; ABS, acrylonitrile butadiene styrene; PC, polycarbonate.

REFERENCES

(1) *Biomaterials Science*, 4th ed.; Wagner, W. R., Sakiyama-Elbert, S. E., Zhang, G., Yaszemski, M. J., Eds.; Elsevier, 2020. https://doi.org/10.1016/C2017-0-02323-6.

(2) McMahon, T. T.; Zadnik, K. Twenty-Five Years of Contact Lenses. *Cornea* **2000**, *19* (5), 730–740. https://doi.org/10.1097/00003226-200009000-00018.

(3) Hoshi, R. A.; van Lith, R.; Jen, M. C.; Allen, J. B.; Lapidos, K. A.; Ameer, G. The Blood and Vascular Cell Compatibility of Heparin-Modified EPTFE Vascular Grafts. *Biomaterials* **2013**, *34* (1), 30–41. https://doi.org/10.1016/j.biomaterials.2012.09.046.

(4) Karamanlioglu, M.; Robson, G. D. The Influence of Biotic and Abiotic Factors on the Rate of Degradation of Poly(Lactic) Acid (PLA) Coupons Buried in Compost and Soil. *Polymer Degradation and Stability* **2013**, *98* (10), 2063–2071. https://doi.org/10.1016/j.polymdegradstab.2013.07.004.

(5) Crawford, L.; Wyatt, M.; Bryers, J.; Ratner, B. Biocompatibility Evolves: Phenomenology to Toxicology to Regeneration. *Advanced Healthcare Materials* **2021**, *10* (11), 2002153. https://doi.org/10.1002/adhm.202002153.

(6) Motlagh, D.; Allen, J.; Hoshi, R.; Yang, J.; Lui, K.; Ameer, G. Hemocompatibility Evaluation of Poly(Diol Citrate)in Vitro for Vascular Tissue Engineering. *Journal of Biomedical Materials Research Part A* **2007**, *82A* (4), 907–916. https://doi.org/10.1002/jbm.a.31211.

(7) Ward, C. P.; Reddy, C. M. Opinion: We Need Better Data about the Environmental Persistence of Plastic Goods. *Proceedings of the National Academy of Sciences* **2020**, *117* (26), 14618–14621. https://doi.org/10.1073/pnas.2008009117.

(8) Ward, C. P.; Armstrong, C. J.; Walsh, A. N.; Jackson, J. H.; Reddy, C. M. Sunlight Converts Polystyrene to Carbon Dioxide and Dissolved Organic Carbon. *Environmental Science & Technology Letters* **2019**, *6* (11), 669–674. https://doi.org/10.1021/acs.estlett.9b00532.

(9) Lu, R. X. Z.; Radisic, M. Organ-on-a-Chip Platforms for Evaluation of Environmental Nanoparticle Toxicity. *Bioactive Materials* **2021**, *6* (9), 2801–2819. https://doi.org/10.1016/j.bioactmat.2021.01.021.

(10) Lehner, R.; Weder, C.; Petri-Fink, A.; Rothen-Rutishauser, B. Emergence of Nanoplastic in the Environment and Possible Impact on Human Health. *Environmental Science & Technology* **2019**, *53* (4), 1748–1765. https://doi.org/10.1021/acs.est.8b05512.

(11) Wright, S. L.; Kelly, F. J. Plastic and Human Health: A Micro Issue? *Environmental Science & Technology* **2017**, *51* (12), 6634–6647. https://doi.org/10.1021/acs.est.7b00423.

(12) Qian, J.; Berkland, C. Drug Release Kinetics from Nondegradable Hydrophobic Polymers Can Be Modulated and Predicted by the Glass Transition Temperature. *Advanced Healthcare Materials* **2021**, 2100015. https://doi.org/10.1002/adhm.202100015.

(13) Galloway, T. S.; Cole, M.; Lewis, C. Interactions of Microplastic Debris throughout the Marine Ecosystem. *Nature Ecology & Evolution* **2017**, *1* (5), 0116. https://doi.org/10.1038/s41559-017-0116.

(14) Fasoli, E. Protein Corona: Dr. Jekyll and Mr. Hyde of Nanomedicine. *Biotechnology and Applied Biochemistry* **2020**, bab.2035. https://doi.org/10.1002/bab.2035.

(15) Amaral-Zettler, L. A.; Zettler, E. R.; Mincer, T. J. Ecology of the Plastisphere. *Nature Reviews Microbiology* **2020**, *18* (3), 139–151. https://doi.org/10.1038/s41579-019-0308-0.

(16) Arnold, J. W.; Roach, J.; Azcarate-Peril, M. A. Emerging Technologies for Gut Microbiome Research. *Trends in Microbiology* **2016**, *24* (11), 887–901. https://doi.org/10.1016/j.tim.2016.06.008.

(17) Stubbins, A.; Law, K. L.; Muñoz, S. E.; Bianchi, T. S.; Zhu, L. Plastics in the Earth System. *Science* **2021**, *373* (6550), 51–55. https://doi.org/10.1126/science.abb0354.