

Materials-based Approaches to Prevent Biofilm-associated Infections

Caitlin Howell, University of Maine

We are already in the post-antibiotic age. The rise of antibiotic resistance is one of the greatest global public health challenges of our time. In the US, more than 2.8 million antibiotic-resistant infections occur each year leading to more than 35,000 deaths.¹ Although new antibiotics continue to be discovered, the pace is slowing while the appearance of new antibiotic-resistant organisms continues to increase at an alarming rate.^{2,3} Addressing this slow-moving crisis will require a coordinated and multi-faceted effort which brings together communities, healthcare facilities, industry, and other stakeholders.¹ However, one target stands out as particularly critical: the development of new materials that can prevent bacteria from adhering to surfaces, proliferating, and forming biofilms, resulting in the reduction of infections before they begin.

Nature's approaches to controlling bacteria. Over millions of years, Nature has developed multiple ways to direct or stop bacterial growth on surfaces, leading to antimicrobial mechanisms which are elegant, effective, and difficult for microorganisms to develop resistance against. For example, cicada⁴ and dragonfly⁵ wings are covered with nanopillar arrays that rupture the membranes of bacterial cells. Lotus plants have hierarchically structured, wax-covered bumps on the surfaces of their leaves which water droplets simply roll off of, cleaning away any adherent microorganisms in the process.⁶ The scales of the Mako shark are patterned in such a way that water flowing over them as the shark swims creates vortices, making it more difficult for bacteria to adhere.⁷ Pilot whale skin has a nanopatterned surface that is perfused with an enzyme-laden gel that breaks the chemical bonds of organisms attempting to adhere.⁸ These are only a few of the myriad ways that Nature controls the adhesion of bacteria on surfaces. However, nearly all of these solutions are made to function under the specific environmental conditions of the animal or plant which makes use of them; thus, they are not always suitable for human applications.

A new way to think about the problem. Recently, interest in another bioinspired antimicrobial solution has been growing: liquid coatings. Inspired by the way that mucosal tissue controls our own large bacterial cohorts, this approach involves the use of a mobile, dynamic, and sacrificial liquid barrier between the microorganisms and the surface which they may contaminate. Critically, the aim with liquid coatings, like our mucosal tissue, is not to kill microorganisms, but rather to change their environment to discourage microbial activity that is harmful, such as forming biofilms.⁹ In proof-of-concept experiments using urinary catheters—one of the most common and infection-prone medical devices^{10–12}—liquid coatings were found to reduce bacterial adhesion by 99% compared to untreated controls. In tests with living systems, liquid coatings performed beyond expectations, reducing not only bacterial adhesion but overall surface protein contamination as well.¹³ Building on this concept, liquid coatings are now being adapted to work with materials that can both sense microorganisms¹⁴ and respond with the application of targeted cleaning,¹⁵ mimicking the way that our tissue is constantly monitoring and responding to the local environment and opening the door to more individually tailored interventions.

Hope for the future. Looking to Nature to inform the development of effective, non-chemical materials strategies to control microorganisms on surfaces is already opening new doors in the race against antibiotic resistance. The further development of these approaches will play a critical role in helping the global community continue adapt to life in the post-antibiotic age.

References

1. Centers for Disease Control and Prevention. The AMR Challenge. <https://www.cdc.gov/drugresistance/intl-activities/amr-challenge.html> (2019).
2. World Health Organization. *Antimicrobial resistance*. <https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance> (2021).
3. World Health Organization. *Global Antimicrobial Resistance Surveillance System*. (2018).
4. Ivanova, E. P. *et al.* Natural Bactericidal Surfaces: Mechanical Rupture of *Pseudomonas aeruginosa* Cells by Cicada Wings. *Small* **8**, 2489–2494 (2012).
5. Bandara, C. D. *et al.* Bactericidal Effects of Natural Nanotopography of Dragonfly Wing on *Escherichia coli*. *ACS Appl. Mater. Interfaces* **9**, 6746–6760 (2017).
6. Barthlott, W. & Neinhuis, C. Purity of the sacred lotus, or escape from contamination in biological surfaces. *Planta* **202**, 1–8 (1997).
7. Choi, W. *et al.* Structural tailoring of sharkskin-mimetic patterned reverse osmosis membranes for optimizing biofouling resistance. *J. Memb. Sci.* **595**, 117602 (2020).
8. Baum, C., Meyer, W., Roessner, D., Siebers, D. & Fleischer, L. G. A zymogel enhances the self-cleaning abilities of the skin of the pilot whale (*Globicephala melas*). *Comp. Biochem. Physiol. Part A Mol. Integr. Physiol.* **130**, 835–847 (2001).
9. Wang, B. X., Wu, C. M. & Ribbeck, K. Home, sweet home: how mucus accommodates our microbiota. *FEBS J.* **288**, 1789–1799 (2021).
10. Reed, D. & Kemmerly, S. a. Infection control and prevention: a review of hospital-acquired infections and the economic implications. *Ochsner J.* **9**, 27–31 (2009).
11. Guggenbichler, J., Assadian, O., Boeswald, M. & Kramer, A. Incidence and clinical implication of nosocomial infections associated with implantable biomaterials – catheters , ventilator-associated pneumonia , urinary tract infections Inzidenz und kli. *GMS Krankenhaushygiene Interdiszip.* **6**, 1–19 (2011).
12. Tambyah, P. A. & Oon, J. Catheter-associated urinary tract infection. *Curr. Opin. Infect. Dis.* **25**, 365–370 (2012).
13. Andersen, M. J. *et al.* Inhibiting host-protein deposition on urinary catheters reduces associated urinary tract infections. *Elife* **11**, (2022).
14. Dixon, B., Sui, C., Briley, A., Hsu, P.-C. & Howell, C. *Continuous, Non-Destructive Detection of Microorganism Growth at Buried Interfaces with Vascularized Polymers*. <https://chemrxiv.org/engage/chemrxiv/article-details/62f67a4342ddf53f75b8d40c> (2022) doi:10.26434/CHEMRXIV-2022-7LT76.
15. Marquis, K. *et al.* Vascularized Polymers Spatially Control Bacterial Cells on Surfaces. *Adv. Biosyst.* **4**, 1–8 (2020).