Nanorobots for concurrent removal of pathogenic bacteria and toxins

IEEE: <https://spectrum.ieee.org/the-human-os/biomedical/devices/bacteria-busters>

Science Magazine: <http://robotics.sciencemag.org/content/3/18/eaat0485>

<https://onlinelibrary.wiley.com/doi/abs/10.1002/adma.201606209> (Dual Cell Coating Technique)

<https://ucsdnews.ucsd.edu/pressrelease/cell_like_nanorobots_clear_bacteria_and_toxins_from_blood>

https://phys.org/news/2016-10-gold-nanowires-biomedical-procedures.html

1. Background
   1. Bacteria problem (Superbugs)
      1. Pathogenetic bacteria
      2. Toxins
   2. Microbots in medicine (Futurism vs Reality)
   3. Main technologies
      1. Magnetic control
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   1. Killing pathogenetic bacteria
   2. Dealing with toxins
3. Future improvements
4. Conclusion

Background

1. Bacteria
   1. Bacteria problem (Superbugs)
      1. The Antibiotic Resistance Crisis

The rapid emergence of resistant bacteria is occurring worldwide, endangering the efficacy of antibiotics, which have transformed medicine and saved millions of lives.[1](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/#b1-ptj4004277)–[6](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/#b6-ptj4004277) Many decades after the first patients were treated with antibiotics, bacterial infections have again become a threat.[7](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/#b7-ptj4004277) The antibiotic resistance crisis has been attributed to the overuse and misuse of these medications, as well as a lack of new drug development by the pharmaceutical industry due to reduced economic incentives and challenging regulatory requirements.[2](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/#b2-ptj4004277)–[5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/#b5-ptj4004277),[8](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/#b8-ptj4004277)–[15](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/#b15-ptj4004277) The Centers for Disease Control and Prevention (CDC) has classified a number of bacteria as presenting urgent, serious, and concerning threats, many of which are already responsible for placing a substantial clinical and financial burden on the U.S. health care system, patients, and their families.[1](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/#b1-ptj4004277),[5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/#b5-ptj4004277),[11](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/#b11-ptj4004277),[16](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/#b16-ptj4004277) Coordinated efforts to implement new policies, renew research efforts, and pursue steps to manage the crisis are greatly needed.[2](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/#b2-ptj4004277),[7](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/#b7-ptj4004277)

*C. difficile* causes life-threatening diarrhea and colitis (an inflammation of the colon), mostly in people who have had both recent medical care and antibiotics

Antibiotics were first used to treat serious infections in the 1940s. Since then, antibiotics have saved millions of lives and transformed modern medicine. During the last 70 years, however, bacteria have shown the ability to become resistant to every antibiotic that has been developed. And the more antibiotics are used, the more quickly bacteria develop resistance.

Anytime antibiotics are used, this puts biological pressure on bacteria that promotes the development of resistance. When antibiotics are needed to prevent or treat disease, they should always be used. But research has shown that as much as 50% of the time, antibiotics are prescribed when they are not needed or they are misused (for example, a patient is given the wrong dose). This not only fails to help patients; it might cause harm. Like every other drug, antibiotics have side effects and can also interact or interfere with the effects of other medicines. This inappropriate use of antibiotics unnecessarily promotes antibiotic resistance.

Antibiotics are a limited resource. The more that antibiotics are used today, the less likely they will still be effective in the future. Therefore, doctors and other health professionals around the world are increasingly adopting the principles of responsible antibiotic use, often called antibiotic stewardship. Stewardship is a commitment to always use antibiotics only when they are necessary to treat, and in some cases prevent, disease; to choose the right antibiotics, and to administer them in the right way in every case. Effective stewardship ensures that every patient gets the maximum benefit from the antibiotics, avoids unnecessary harm from allergic reactions and side effects, and helps preserve the life-saving potential of these drugs for the future. Efforts to improve the responsible use of antibiotics have not only demonstrated these benefits but have also been shown to improve outcomes and save healthcare facilities money in pharmacy costs.

Antibiotic resistance is a worldwide problem.

Each year in the United States, at least 2 million people acquire serious infections with bacteria that are resistant to one or more of the antibiotics designed to treat those infections. At least 23,000 people die each year as a direct result of these antibiotic-resistant infections. Many more die from other conditions that were complicated by an antibiotic-resistant infection.

The total economic cost of antibiotic resistance to the U.S. economy has been difficult to calculate. Estimates vary but have ranged as high as $20 billion in excess direct health care costs, with additional costs to society for lost productivity as high as $35 billion a year (2008 dollars).

The use of antibiotics is the single most important factor leading to antibiotic resistance around the world. Antibiotics are among the most commonly prescribed drugs used in human medicine. However, up to 50% of all the antibiotics prescribed for people are not needed or are not optimally effective as prescribed. Antibiotics are also commonly used in food animals to prevent, control, and treat disease, and to promote the growth of food-producing animals. The use of antibiotics for promoting growth is not necessary, and the practice should be phased out. Bacteria will inevitably find ways of resisting the antibiotics we develop, which is why aggressive action is needed now to keep new resistance from developing and to prevent the resistance that already exists from spreading.

Because antibiotic resistance occurs as part of a natural evolution process, it can be significantly slowed but not stopped. Therefore, new antibiotics will always be needed to keep up with resistant bacteria as well as new diagnostic tests to track the development of resistance.

* 1. How Bacteria affect blood
  2. How toxins of the bacteria affect blood

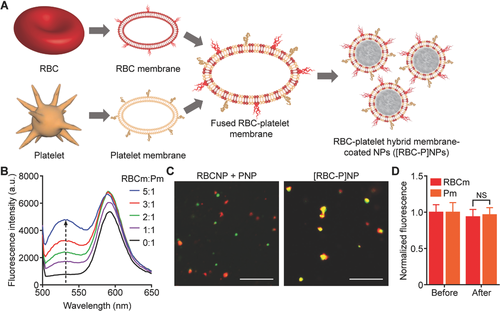
1. Micro- & Nanobots
   1. Modern-day applications
   2. Main technologies involved
   3. Examples

Approach-Replicating Cell membrane (Title)

Single cell membranes coat the nanodevices and mimic the functions and properties of the source sells and bear unique functions

* For instance, lipid membranes separate and filter the inner contents of the cell from outside forces and is a protection barrier
* These functions can also be disease-relevant targeting ability.
* RBC-PL membrane coating of nanorobots
  + New Experiment of fusing two membranes to create a variety of functional proteins and multifaceted biological functions.
  + platelets, which bind pathogens bacteria and red blood cells, which absorb and neutralize the toxins produced by these bacteria.
  + dynamic movement of mobile robotics
  + functional versatility of the cellular membrane coatings.

Developed cell membrane -

* “acoustic gold nanowire (AuNW)–
* based nanorobot used as a model of fuel-free robot with potential biomedical applications”
* Why AuNW? Well I'll tell you! red blood cells measure about 7 micrometers. Because the wire is so small, it can pierce a biological cell to stimulate the cell membrane and investigate its interior
* AuNW electrochemical deposition protocol
  + How membranes are created through electric current to reduce dissolved metal cations so that they form a thin coherent metal coating on an electrode
  + This approach ‘template synthesis’ because the pores within these nanoporous membranes act as templates for the synthesis of nanostructures of the desired material. It’s like setting up the tree before putting the ornaments on
  + Electrochemical deposition works because of some very fundamental electrochemical properties. Two electrodes, an anode and a cathode, are dipped into an electrolytic solution. Electrode and electrolyte material selection are incredibly important during this process.
  + To give a material a protective coating
  + gold deposition within the nanopores of a polycarbonate membrane, followed by the membrane dissolution and release of the resulting AuNWs. The surface of the AuNWs modified with 3-mercaptopropionic acid before membrane coating
* dual–cell membrane–cloaking technique
  + fusion of the RBC and PL membranes -during a 5-min ultrasonication.
  + The resulting RBC-PL-vesicles, having diverse biological capabilities, were mixed with the MPA-modified AuNWs under ultrasonication for 5 min and due to high surface tension energy were prone to bind with it.

Movement: Ultrasound

* Device with multiple functions due to hybrid membrane that detoxifies RBC and moves around with targets and does not need any other external mechanical forces
* produced a synergistic effect of enhancing mass transport
* “Samples treated with acoustically-propelled robots produce a 2.4-fold lower rupture of red blood cells and a 3.5-fold increase in bacteria binding, compared with static nanorobots.”
* “A 4.5 times lower hemolysis was found when using US-propelled RBC-PL-robots compared with the use of the RBC-PL-robots under static conditions”
* Tested blood vs water (bare robot)
  + the bare robots displayed notable hindered propulsion, with a greatly diminished speed of ~10 μm s−1, nearly independent of the incubation time (right after mixing and after 1-hour incubation in blood) This hindered movement reflects severe protein fouling of the robots.
* Tested water vs blood (robot with RBC-PL membranes)
  + no biofouling, and mimicked natural motile cells
  + The protein profile of the coated robots closely matched that of the hybrid membranes, indicating that the RBC-PL membranes can be translocated onto the nanorobot surface without altering their protein profile.

methicillin-resistant *Staphylococcus aureus* -model pathogen and α-toxin as well as other PFTs secreted by MRSA bacteria as model toxins

* + - RBC-PL-robots were added to the bacterial suspension under a US field for 5 min. After the robot treatment, the robots were magnetically separated from the bacterial suspension.
    - RBC-PL-robots offer simultaneous accelerated detoxification of different bio contaminants present in the same sample within minutes.
    - “This hybrid cell membrane coating allows the nanorobots to perform the tasks of two different cells at once—platelets, which bind pathogens like MRSA bacteria (an antibiotic-resistant strain of Staphylococcus aureus), and red blood cells, which absorb and neutralize the toxins produced by these bacteria. The gold body of the nanorobots responds to ultrasound, which gives them the ability to swim around rapidly without chemical fuel. This mobility helps the nanorobots efficiently mix with their targets (bacteria and toxins) in blood and speed up detoxification.”

Development

* “ So far, only singular cell membranes have been coupled with nanorobots, providing them with the specific biological function of the corresponding cells while lacking multifaceted functionality. The integration of diverse membrane functionalities from multiple cell types into single mobile nanorobots could result in broader and more robust uses, where the nanorobots could perform multiple complex therapeutic tasks in a single treatment.”
* “This dual–cell membrane coating represents a unique and robust technique to functionalize nanorobots for potential use in different fields, including targeted drug delivery, immune modulation, and detoxification.”