

Alternating Magnetic Fields (AMF) and Antibiotics Eradicate Biofilm on Metal in a Synergistic Fashion



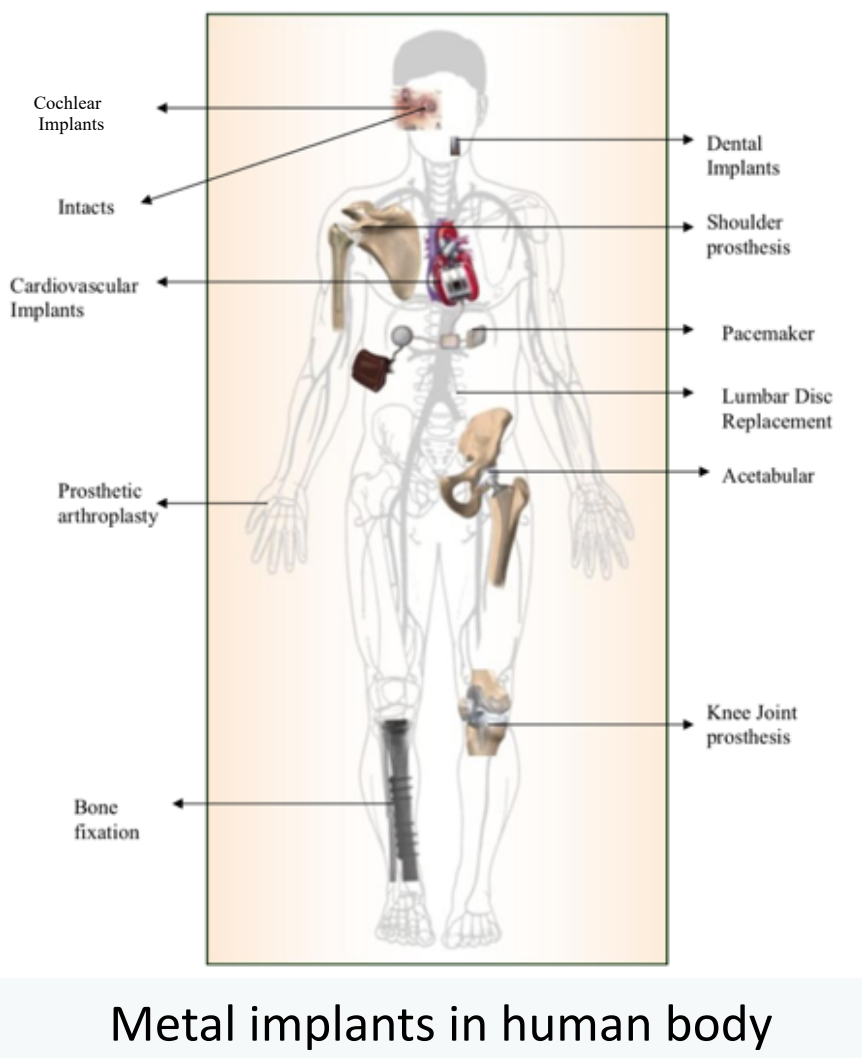
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Introduction

Infections Related to Metal Implants

Millions of devices are implanted annually such as prosthetic joints, bone fixation hardware (screws, plates, rods), and dental implants. However, there are a percentage of procedures that have complications with one of the most serious being infection. To treat such infections, surgical intervention is often required, which causes significant morbidity and is costly to the healthcare system.

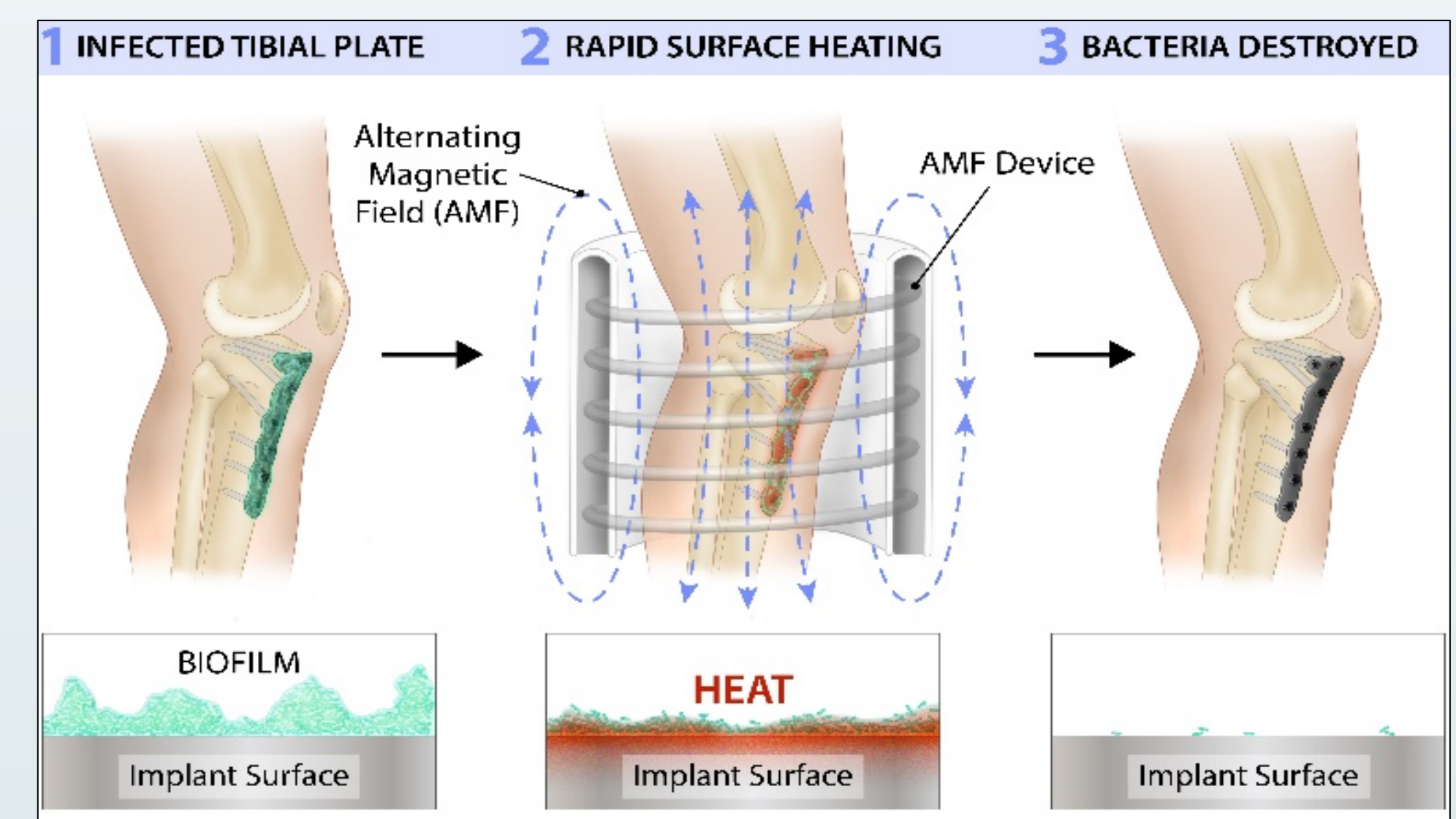


Biofilm in Metal Implant Infection

Bacterial biofilms, an aggregate of bacteria and extracellular polymeric substances (EPS) on the implant surface, are associated with most of the infections. The existence of biofilm, only tens to hundreds micrometer-thick, makes the bacteria much more resistant to the antibiotics and immune system when compared to planktonic bacteria.

Non-Invasive Treatment using Alternating Magnetic Fields

Our group is developing a non-invasive method to treat metal implant infections (MII) using alternating magnetic fields (AMF). The treatment is based on the principle of using magnetic induction to non-invasively heat the metal prostheses and destroy the biofilm. Biofilm showed effective elimination over different temperature ranges and heat treatment times.

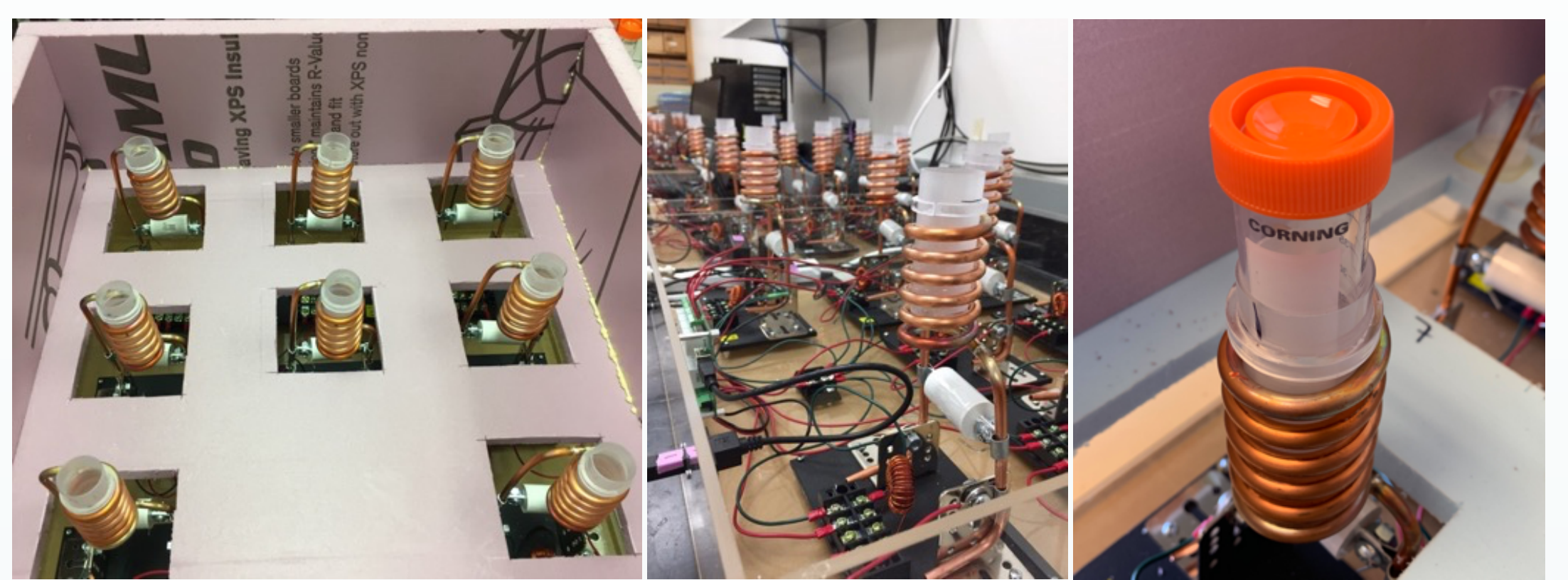


The concept of treating Metal Implant Infection using AMF. The AMF is generated by the coil around the metal implant.

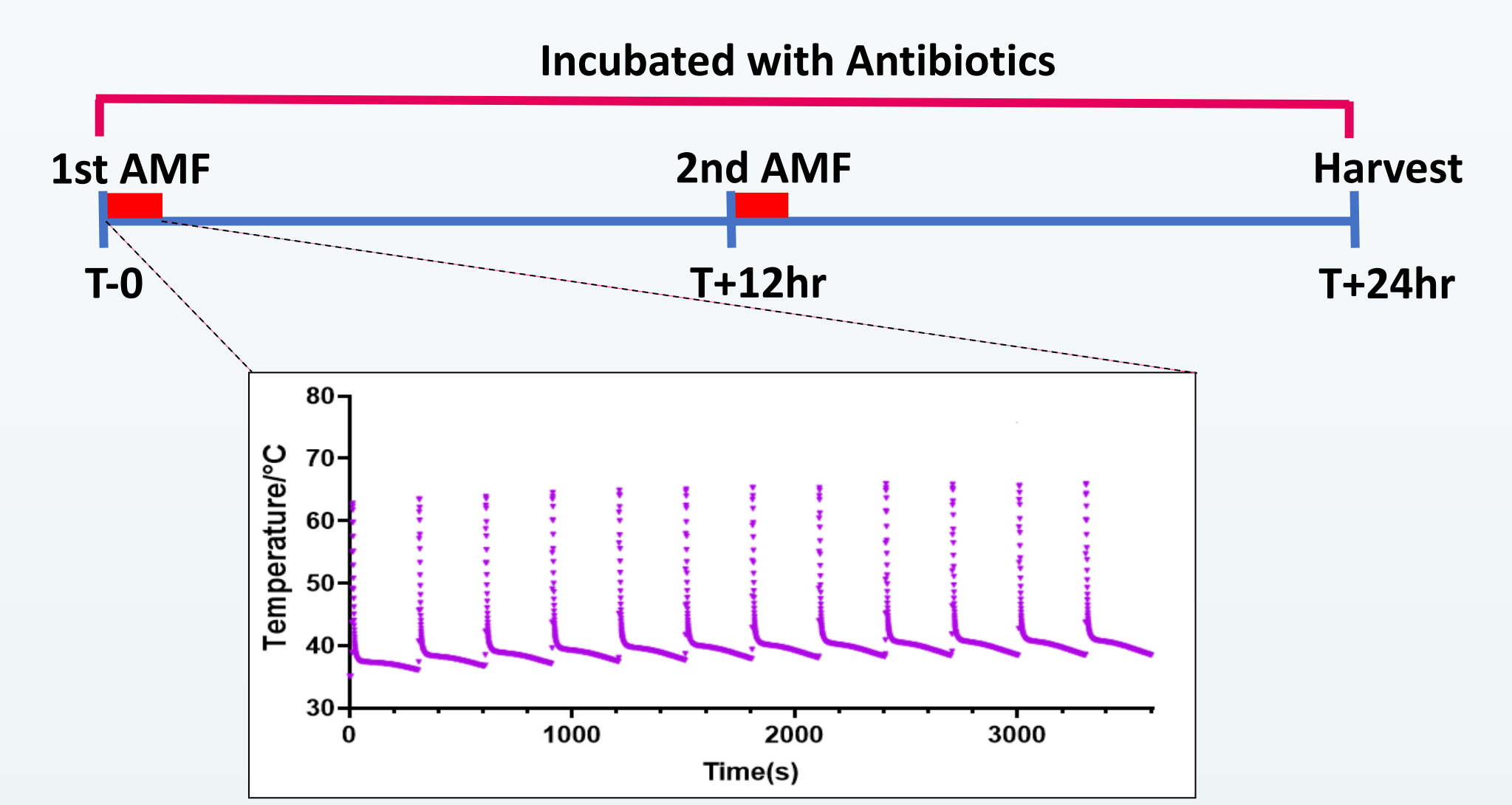
Objective

- Develop novel tools and methods to eradicate biofilm on metal implants non-invasively
- Investigate the interaction of AMF and antibiotics to biofilms

Device and Methods

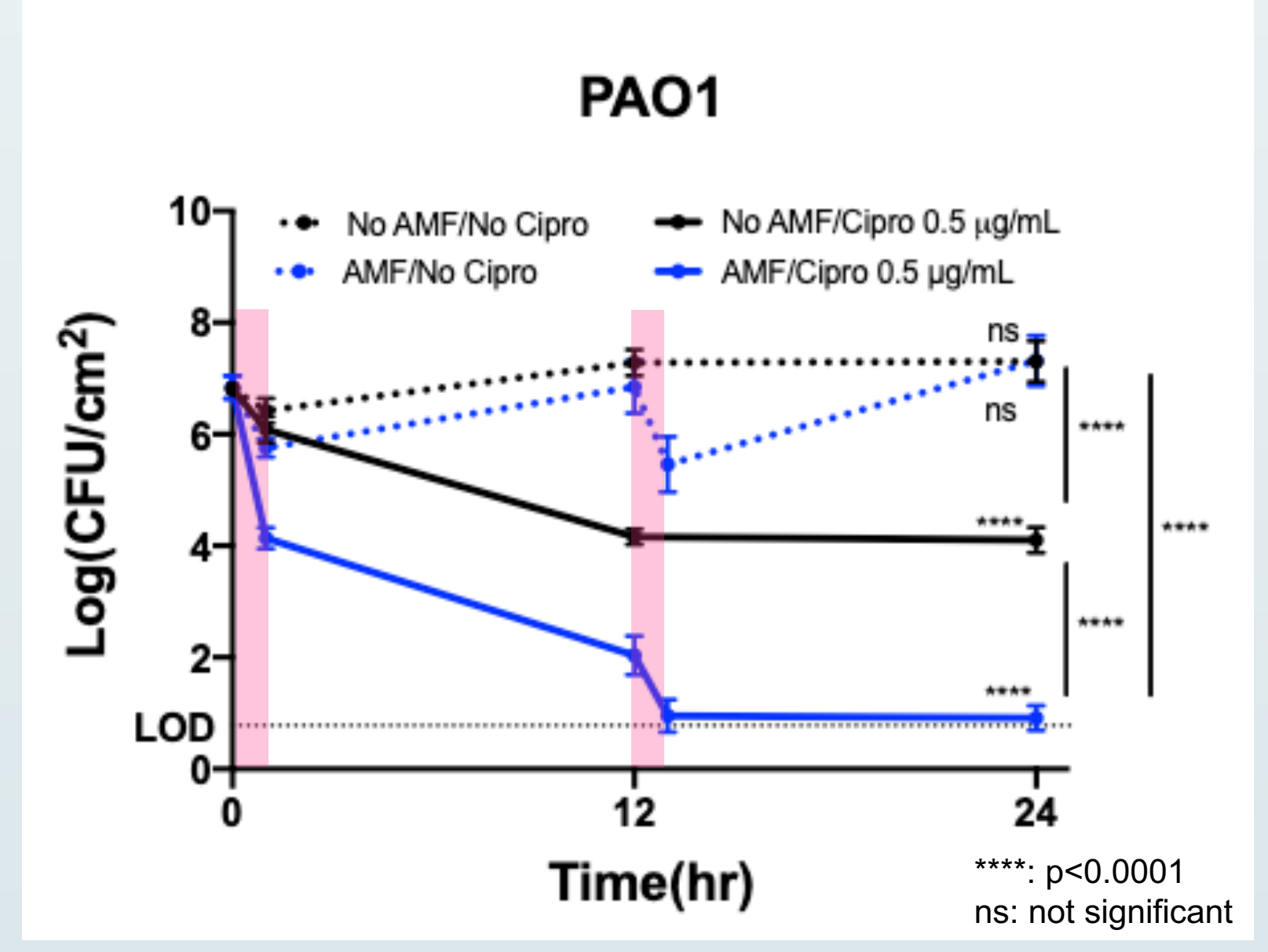


The "coil farm" in the lab for AMF treatment of biofilms



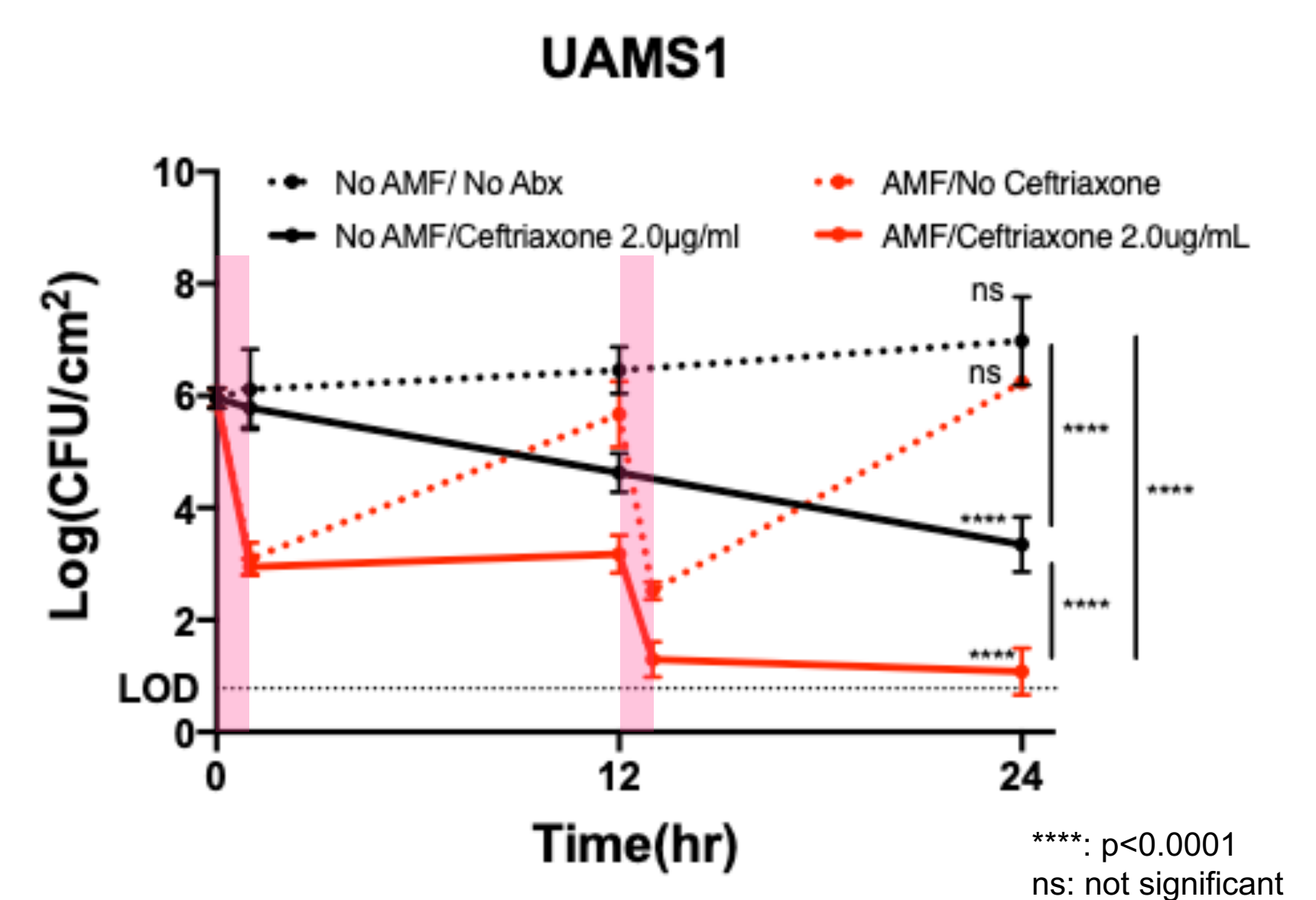
The time sequence of AMF treatments. In 1 hr AMF session, the coil was able to deploy 12 individual 3 s AMF pulse, which would raise the temperature to ~65 °C. The 5 min interval was sufficient time between exposures for the ring to return to baseline temperature. The AMF treatments were conducted at 0 hr and 12 hr.

P. aeruginosa (PAO1) Treated with AMF and Ciprofloxacin



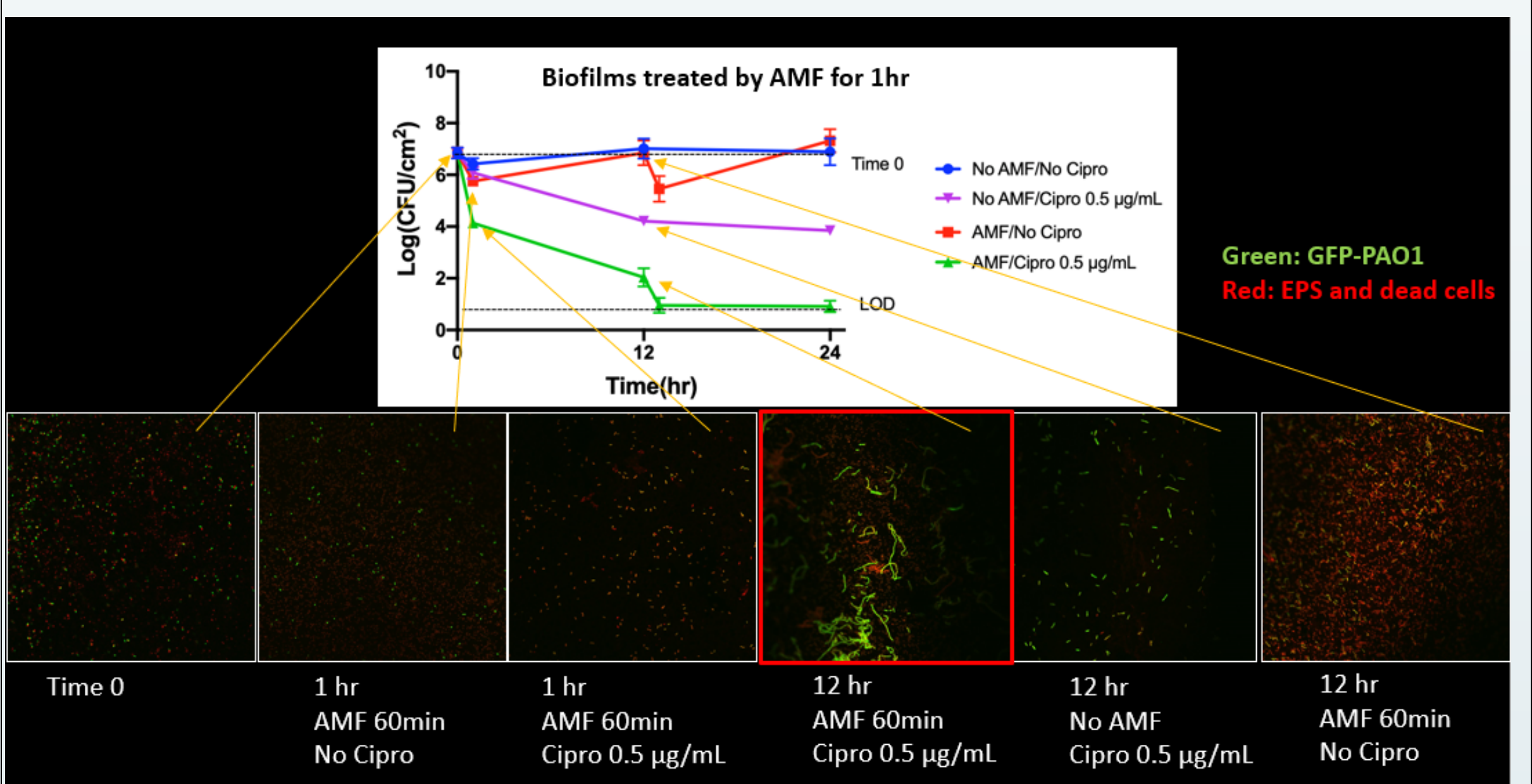
P. aeruginosa (PAO1) biofilm treated with AMF at time 0 hr and 12 hr, incubated in the presence and absence of ciprofloxacin. The AMF treatment time was 1 hr, as shown by the colored bars. The result showed that combining AMF and antibiotics resulted in elimination of biofilm after multiple AMF treatments.

S. aureus (UAMS1) Treated with AMF and Ceftriaxone



S. aureus (UAMS1) biofilm treated with AMF at time 0 hr and 12 hr, incubated in the presence or absence of ceftriaxone. The AMF treatment time was 1 hr. The result showed that combining AMF and antibiotics resulted in elimination of biofilm after multiple AMF treatments.

Microscopy



Microscopy of the *P. aeruginosa* biofilm under AMF and antibiotic treatment. Prolongated cells were showed in the graph with AMF treatment and antibiotics incubation at 12 hr, suggesting the antibiotics had strong interaction with the bacteria, while no obvious cell prolongation was found in the antibiotics only group.

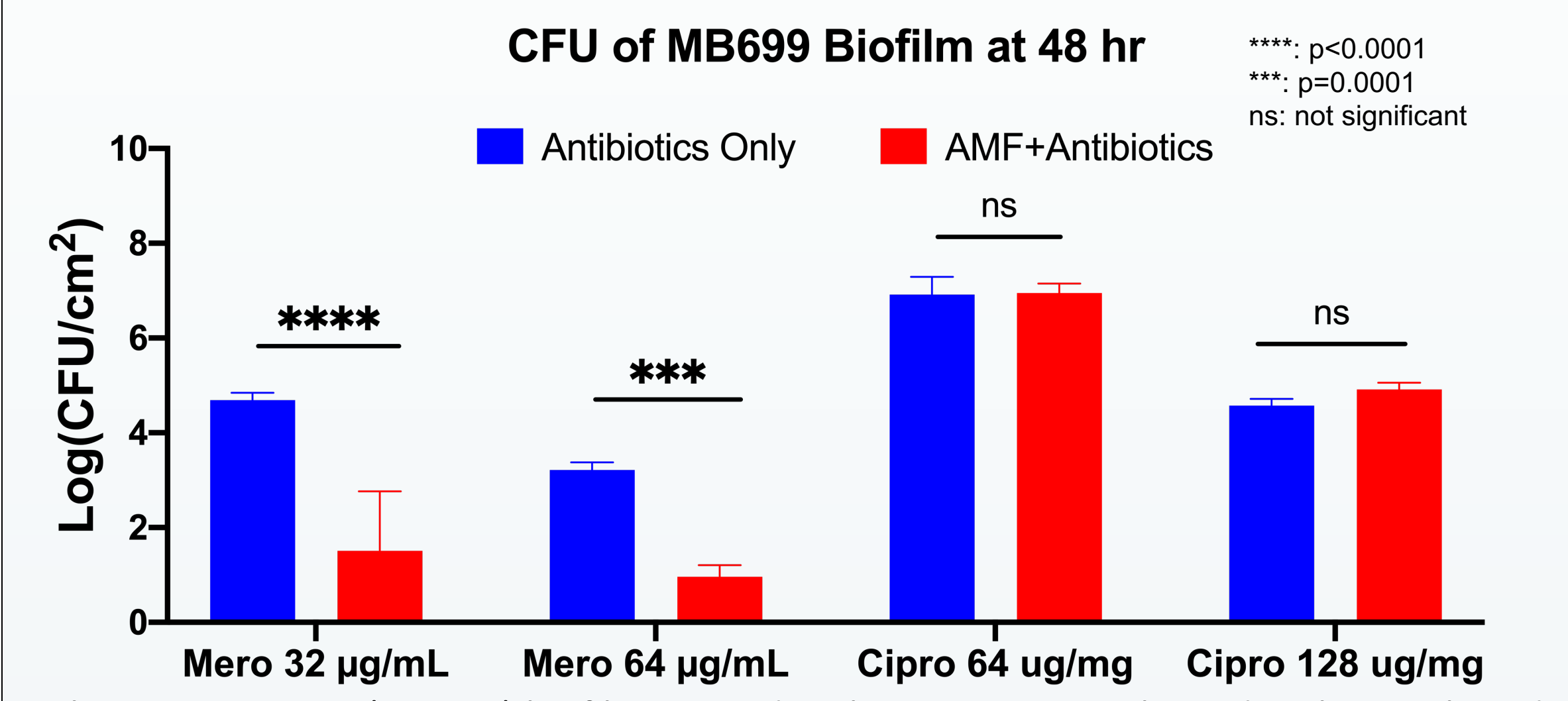
References

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2. Ricker, E. B., Aljaafari, H. A. S., Bader, T. M. & Hundley, B. S. Thermal shock susceptibility and regrowth of *Pseudomonas aeruginosa* biofilms. *Int. J. Hyperth.* 0, 168–176 (2018).
3. Chopra, R. *et al.* Employing high-frequency alternating magnetic fields for the non-invasive treatment of prosthetic joint infections. *Sci. Rep.* 7, 1–14 (2017).

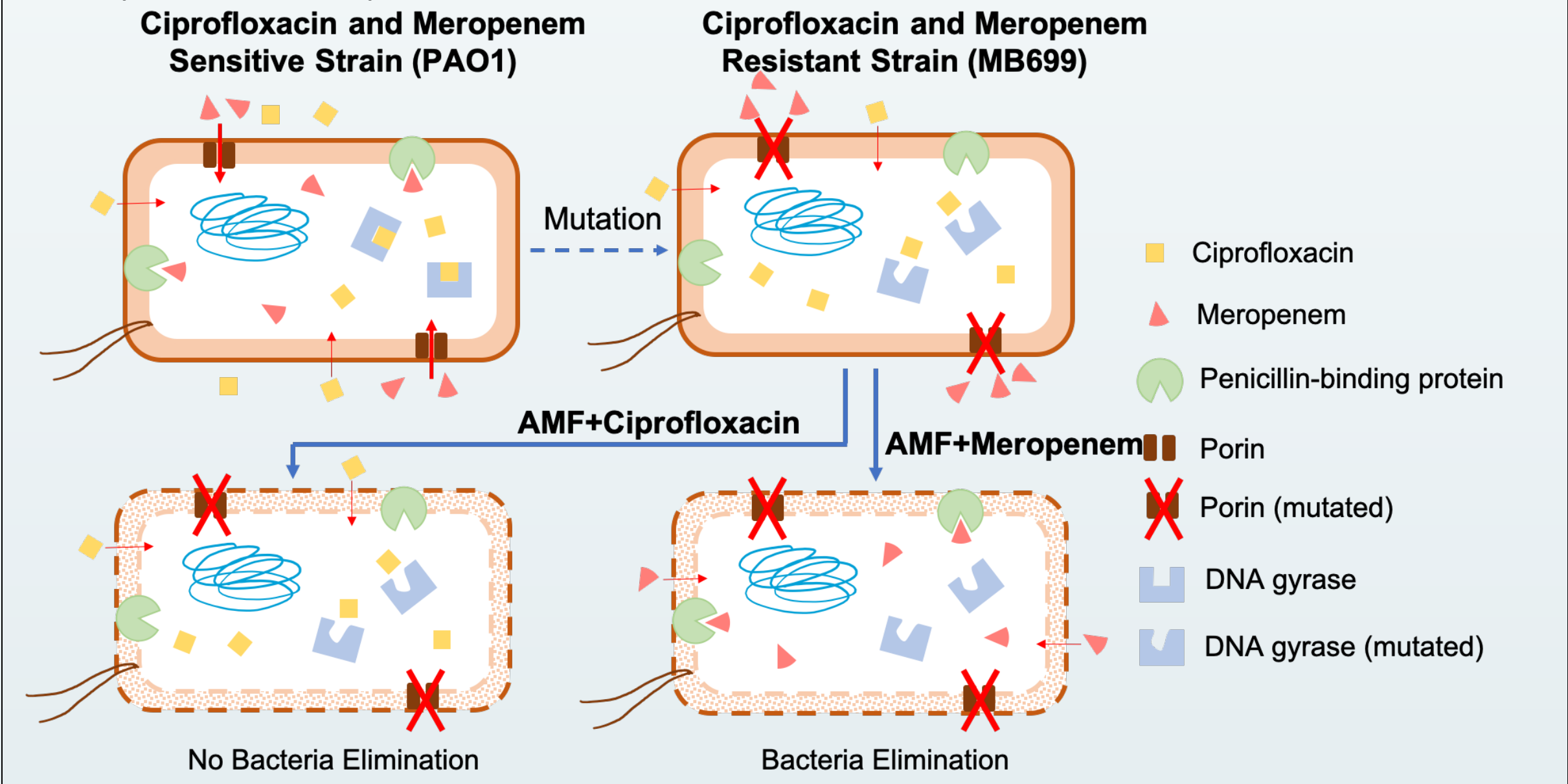
Understanding the Mechanism of Action

Minimum Inhibitory Concentration (MIC) of *P. aeruginosa*

	PAO1	MB699 (resistant strain)
Ciprofloxacin	0.125 µg/mL	64 µg/mL
Meropenem	0.5 µg/mL	64 µg/mL



The *P. aeruginosa* (MB699) biofilm treated with AMF at time 0 hr and 24 hr, incubated with ciprofloxacin or meropenem. The AMF treatment time was 1 hr. At 48 hr, CFU reduction with both meropenem and AMF was significantly larger than meropenem alone, while with both ciprofloxacin and AMF, no significant difference was observed in comparison with ciprofloxacin alone.



MB699 has porin and DNA gyrase mutation. The porin mutation prevents meropenem entering cell, and the mutated DNA gyrase resists ciprofloxacin binding. It suggests that cell integrity was damaged due to AMF, so meropenem had enhanced entry into the cell and bind to the target site, showing enhanced bactericidal effect. Through ciprofloxacin entry was enhanced by AMF, no enhanced bactericidal effect was shown because the binding of Ciprofloxacin to DNA gyrase was still inhibited.

Conclusion

- When combined with antibiotics, AMF displays a synergistic effect in eradicating biofilm.
- This synergy was observed in different pathogens and in multiple antibiotics.
- It suggested that the mechanism of the synergy is related to the enhanced ability of antibiotics to enter the cell by an AMF effect.