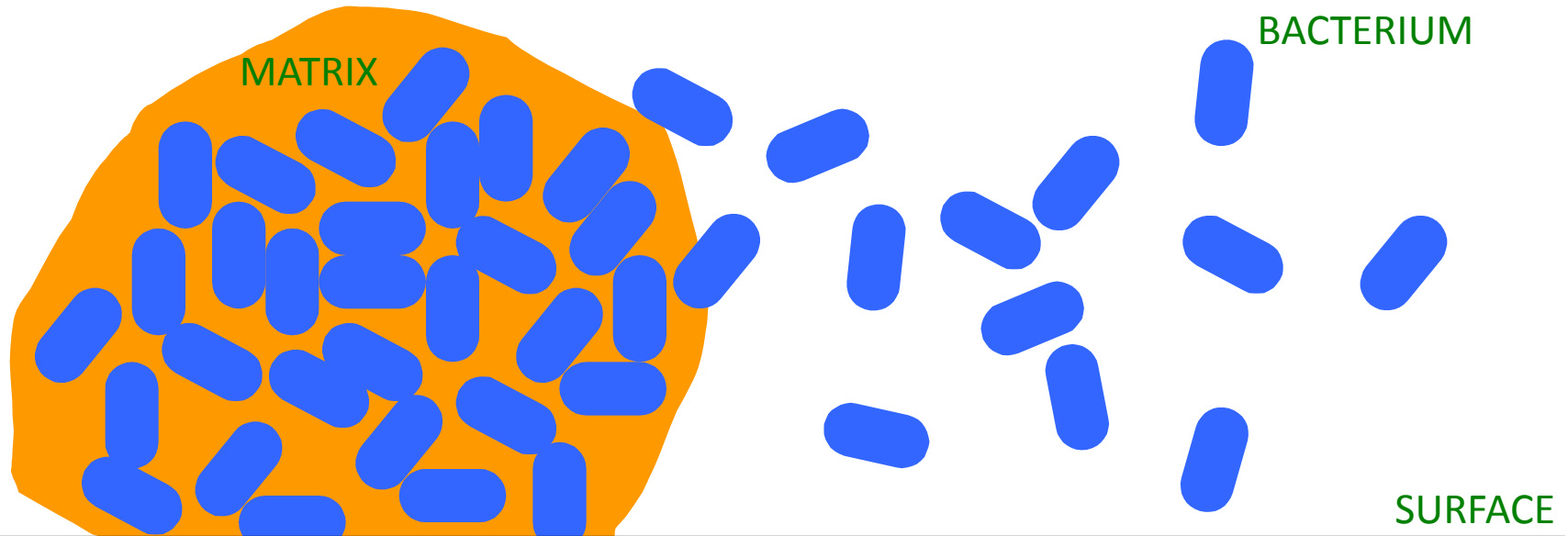


Antibiotic-induced biofilm formation

Jeffrey Kaplan PhD
Department of Biology
American University
Washington DC

What are biofilms?

Biofilms are communities of bacteria, encased in a polymeric matrix, growing attached to a tissue or surface:

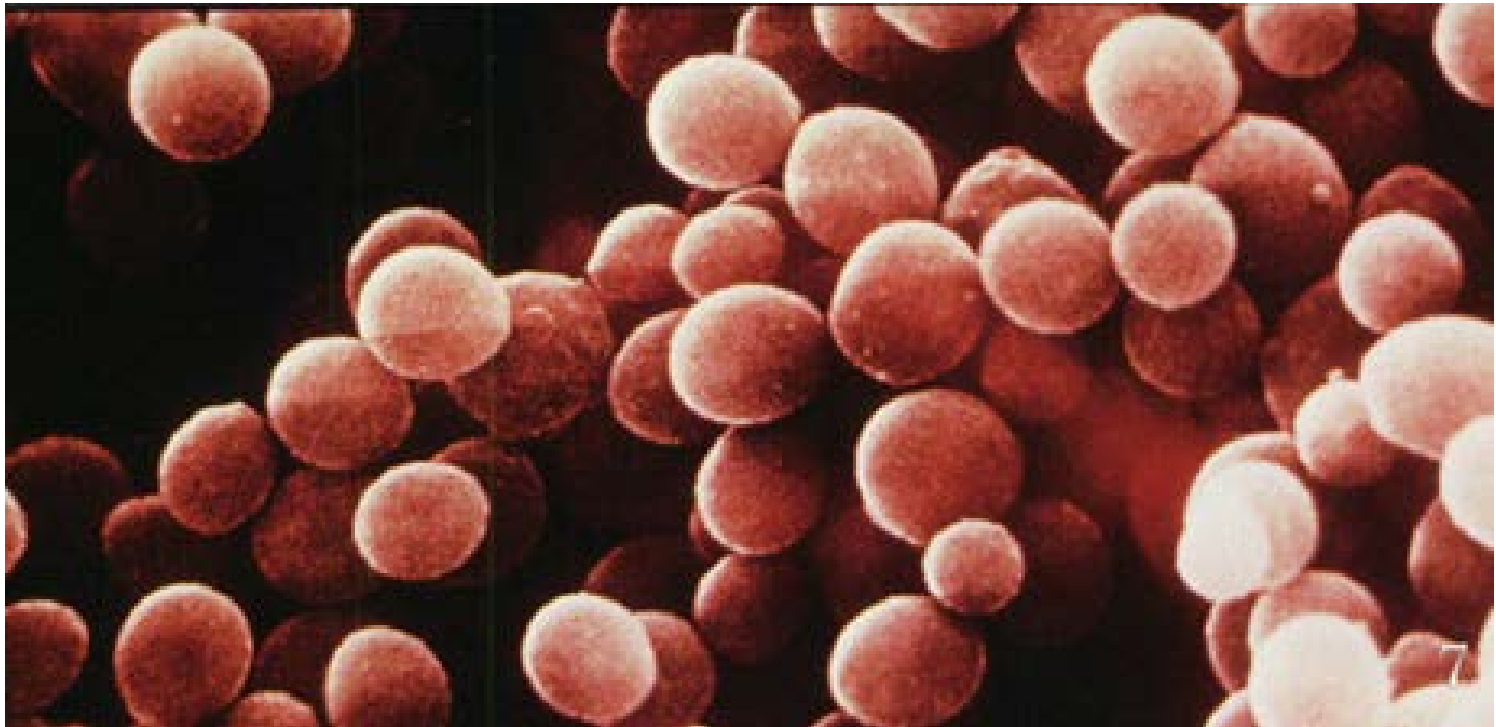


Biofilm colony

Planktonic cells

What is MRSA?

Methicillin-resistant *Staphylococcus aureus* is a bacterium that kills more people in the US than HIV/AIDS



MRSA biofilms contribute to pathogenesis

MRSA biofilms form on medical devices, soft tissue and bone.

Biofilms protects MRSA from killing by host defenses and antibiotics.

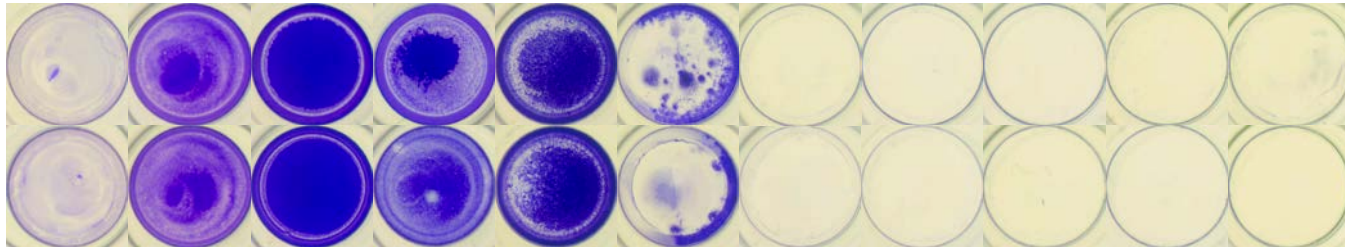
MRSA biofilms are difficult or impossible to eradicate with conventional antibiotics.

Biofilm assay

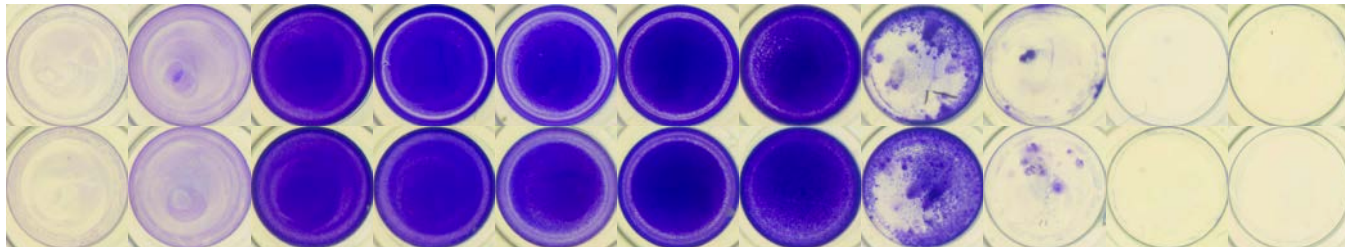
[Methicillin] ($\mu\text{g/ml}$)

0 1 2 3 4 5 6 7 8 9 10

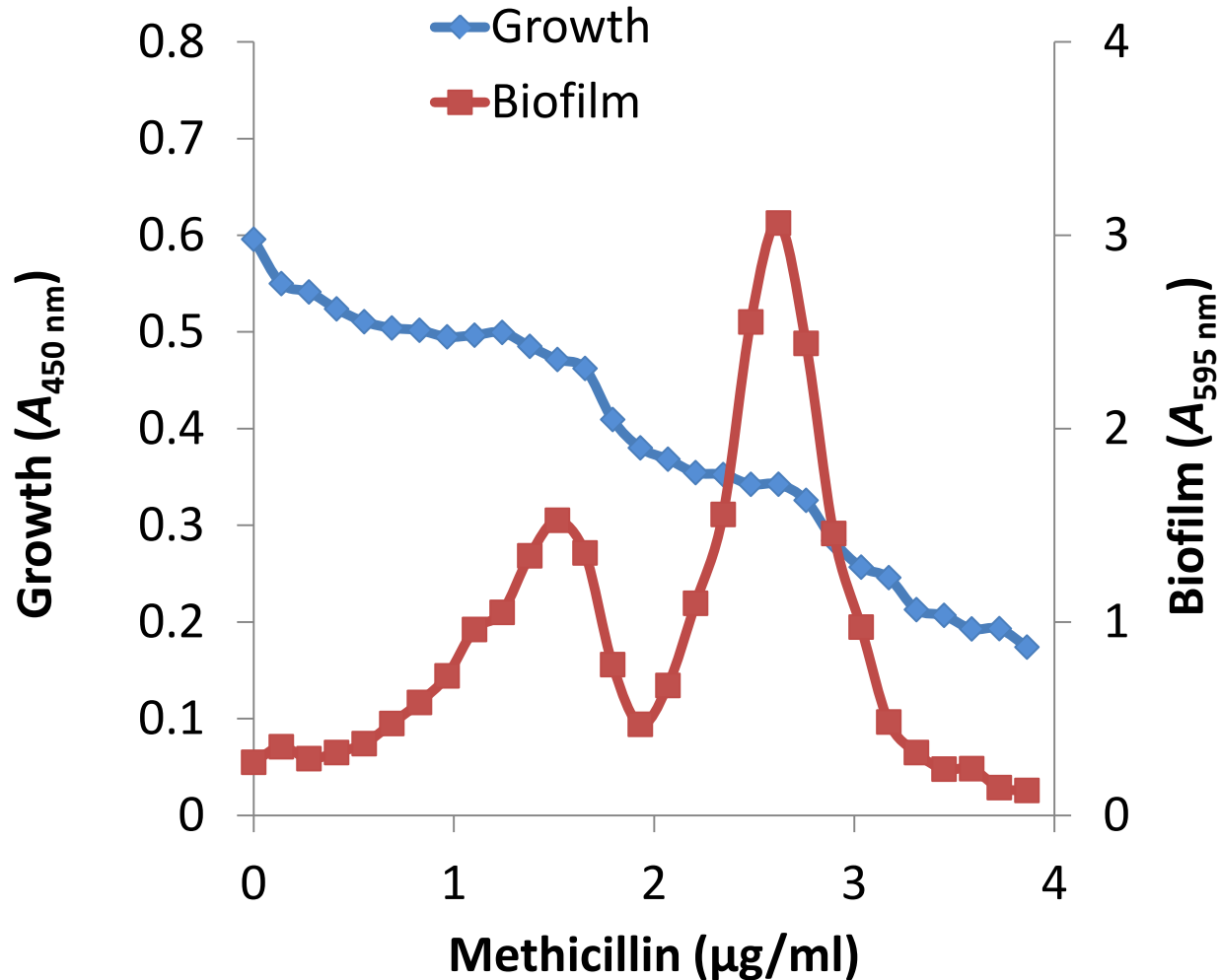
Strain
USA300



Strain
USA500

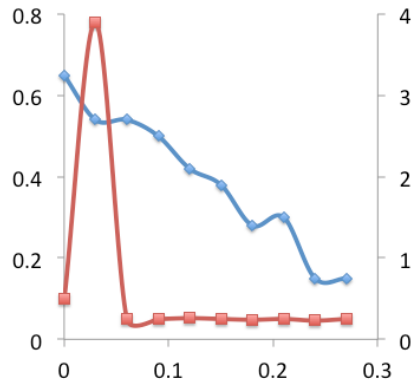


Low levels of methicillin induce MRSA biofilm

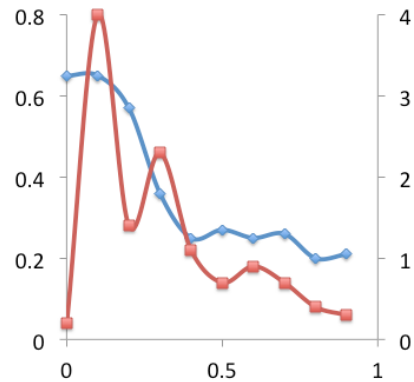


Other β -lactam antibiotics also induce MRSA biofilm

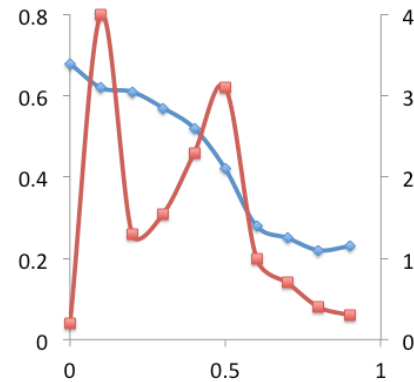
Penicillin



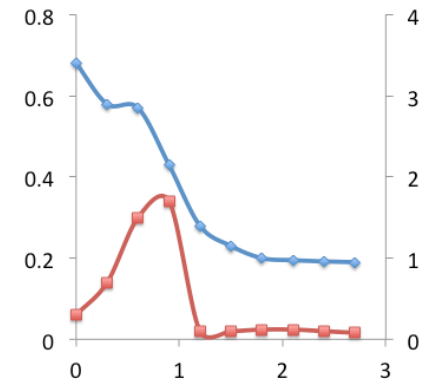
Amoxicillin



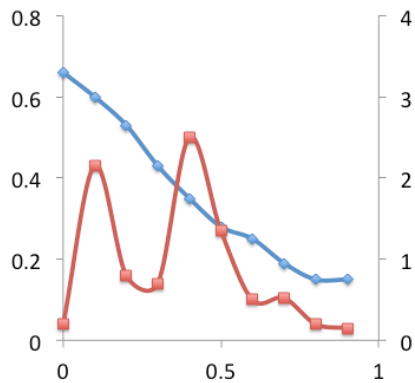
Ampicillin



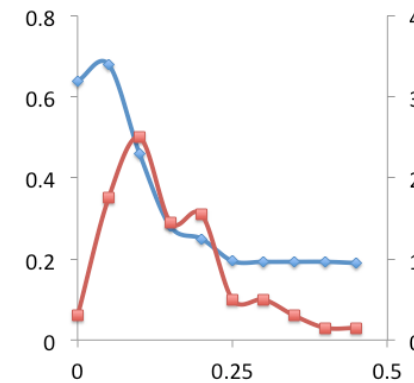
Piperacillin



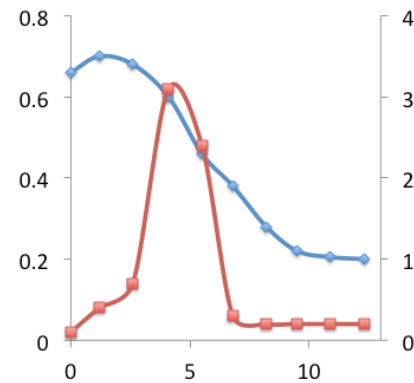
Nafcillin



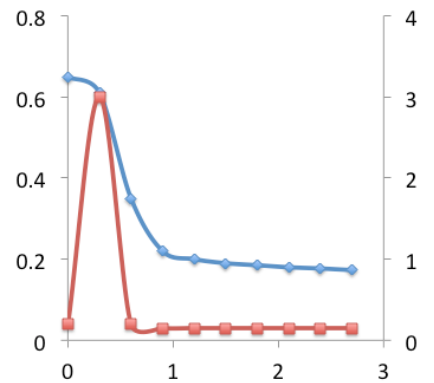
Cloxacillin



Ceftriaxone

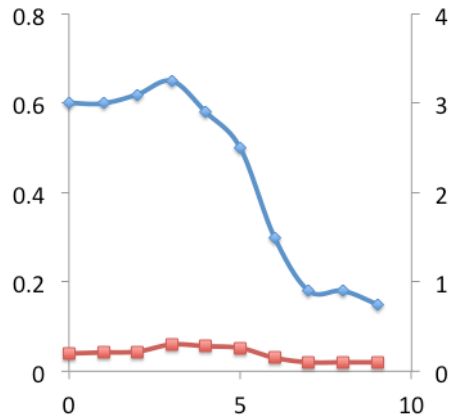


Cefazolin

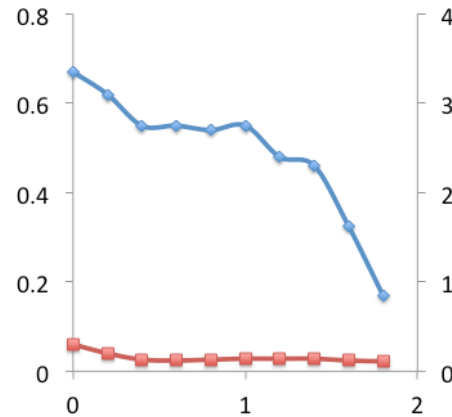


Non- β -lactam antibiotics do not induce MRSA biofilm

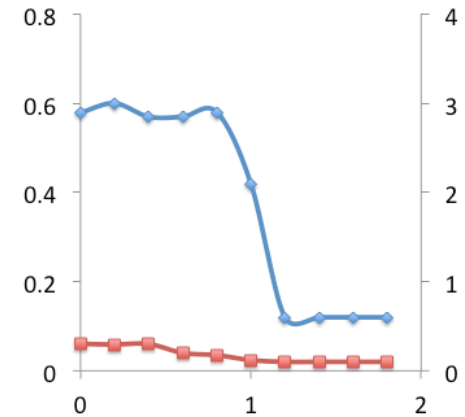
Trimethoprim/
sulfamethoxazole



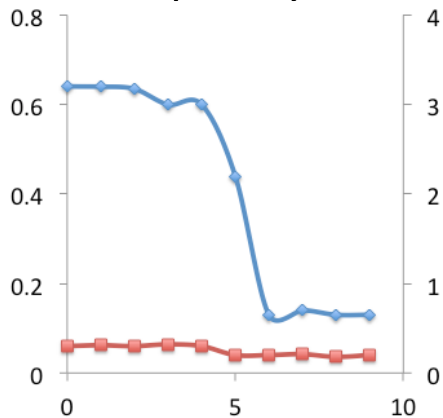
Linezolid



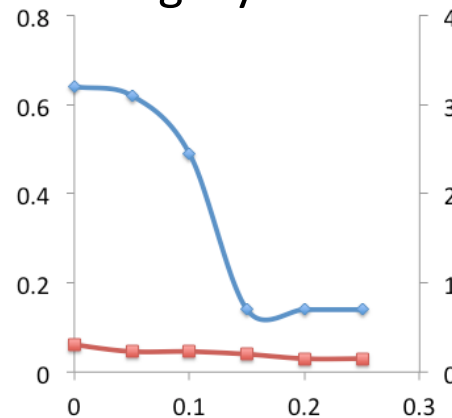
Vancomycin



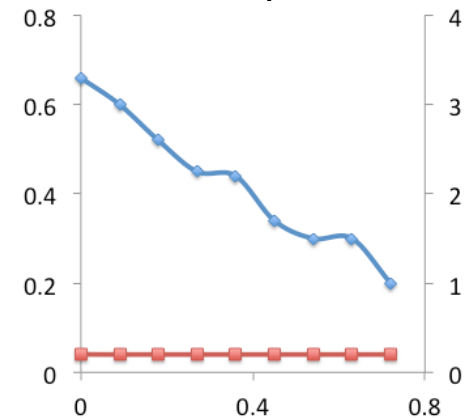
Daptomycin



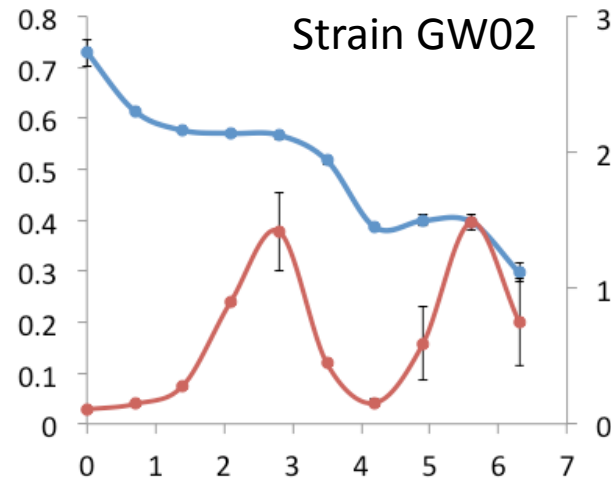
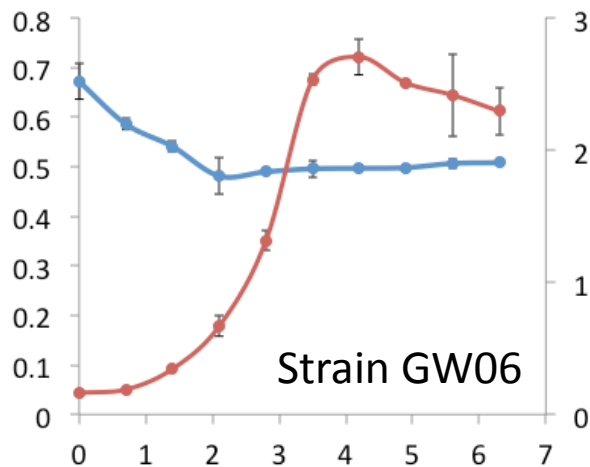
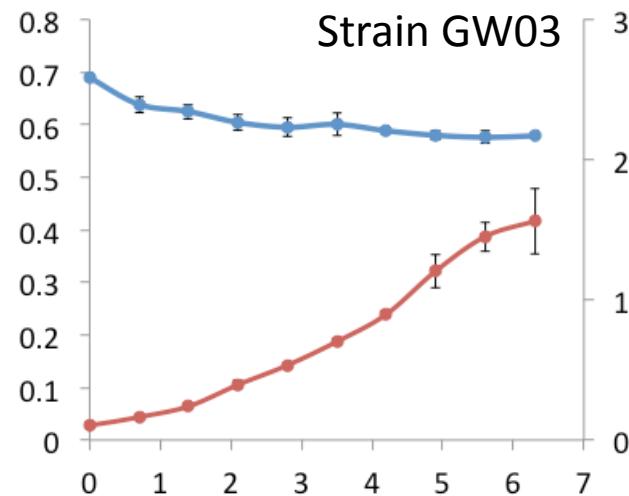
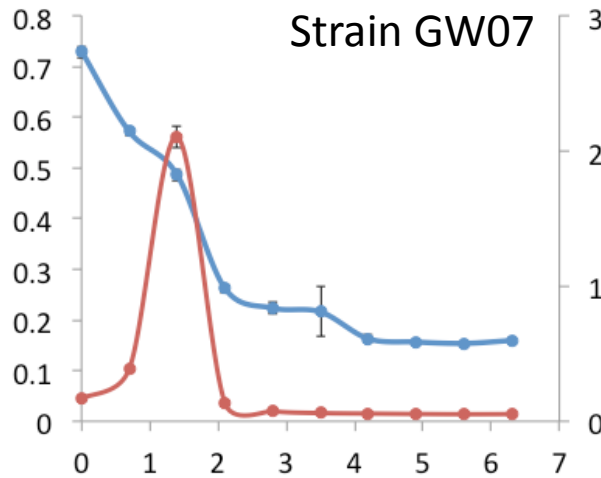
Tigecycline



Rifampicin

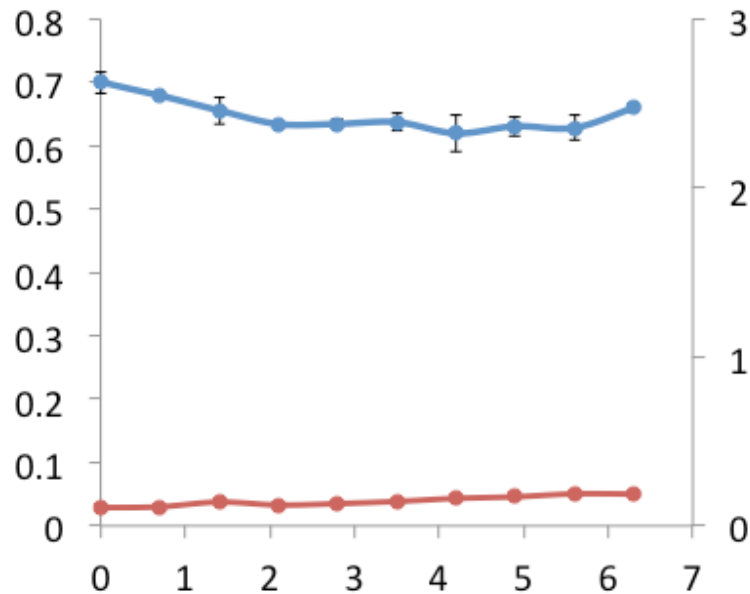


Most MRSA clinical strains (87%) are inducible ...

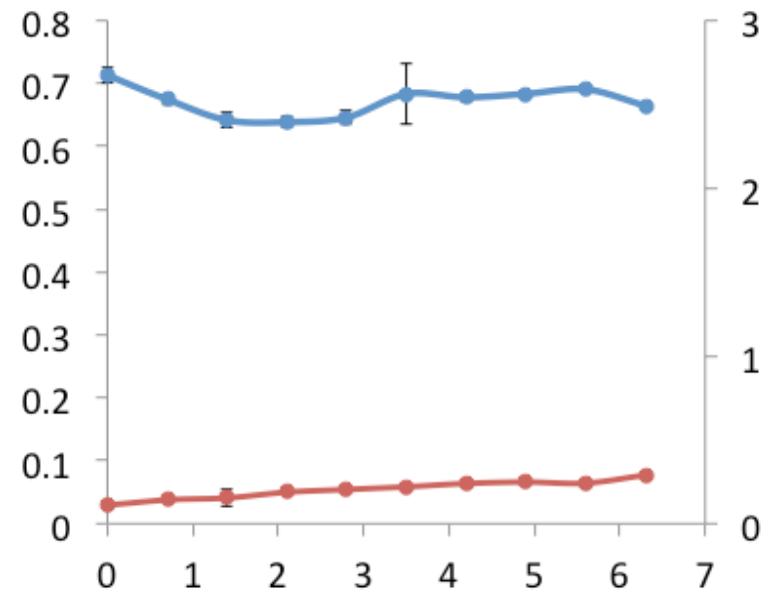


... while some strains are not highly inducible

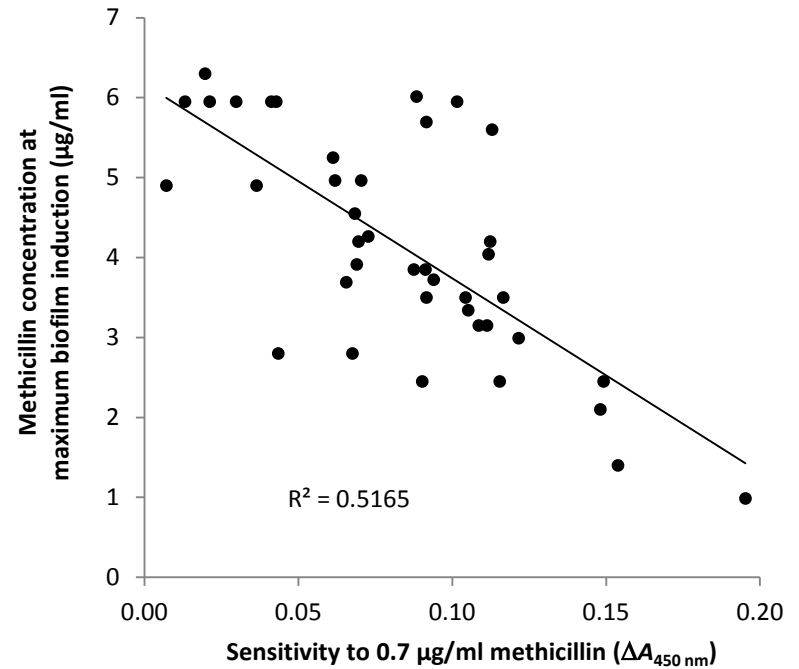
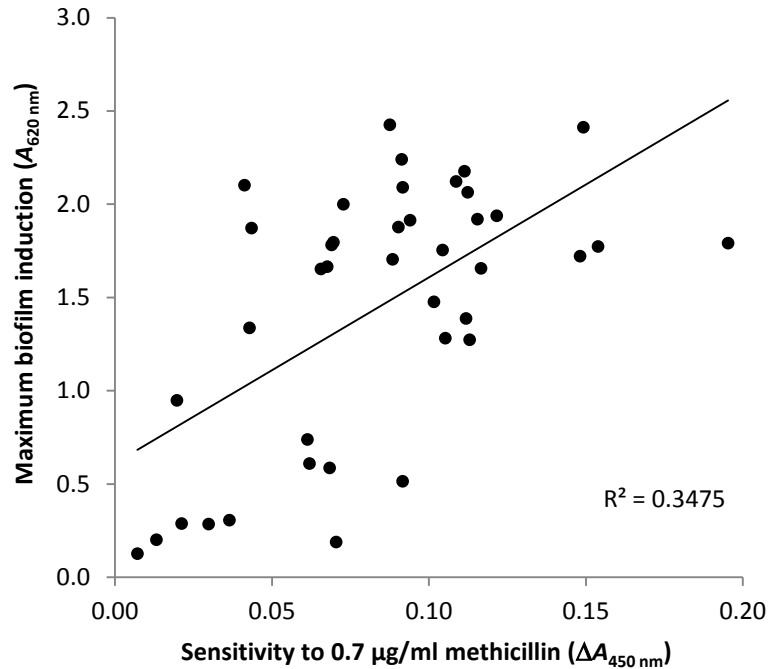
Strain GW04



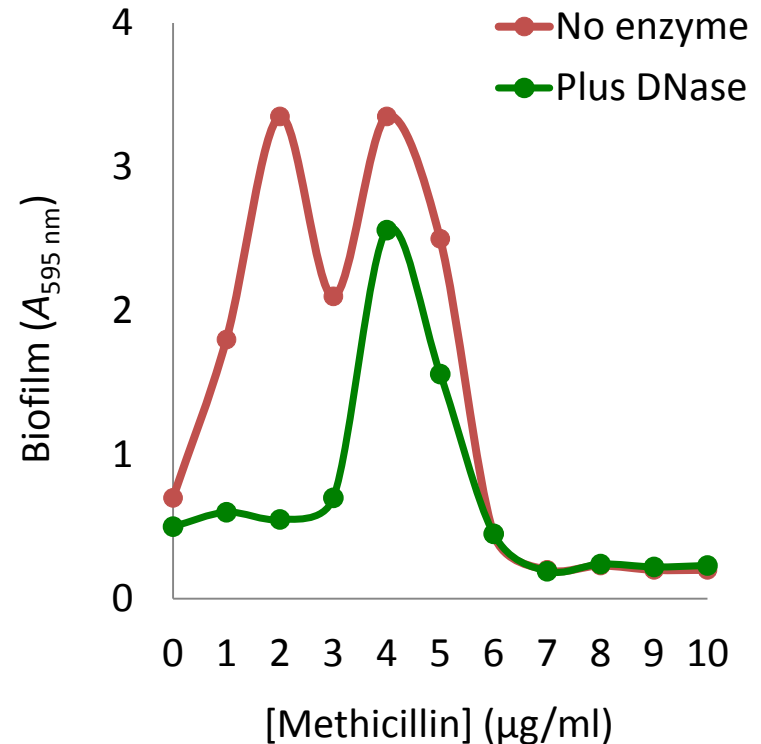
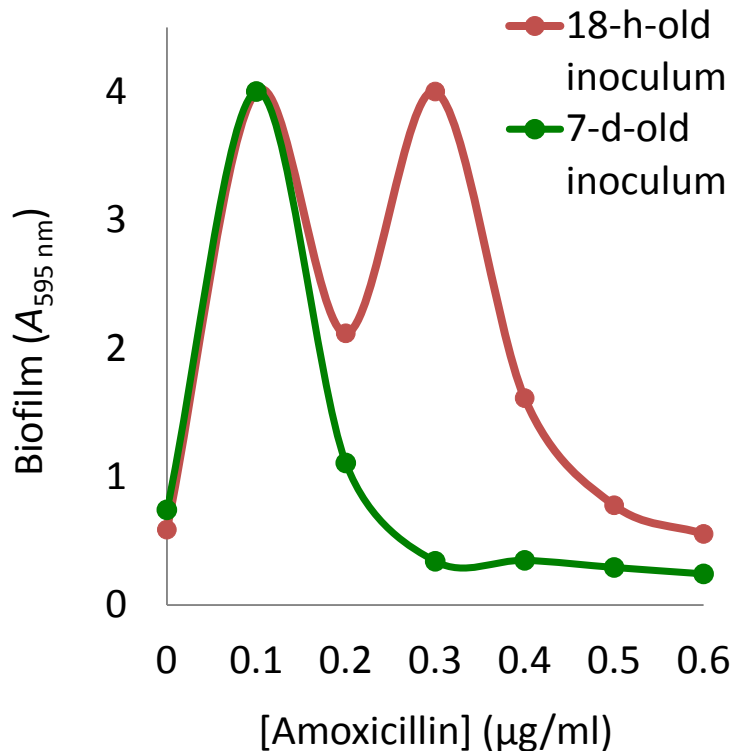
Strain GW09



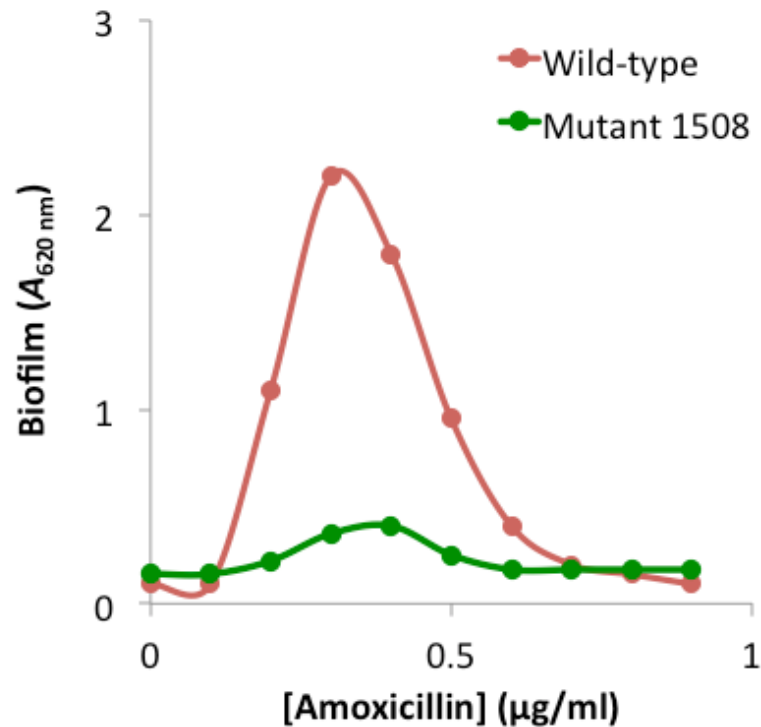
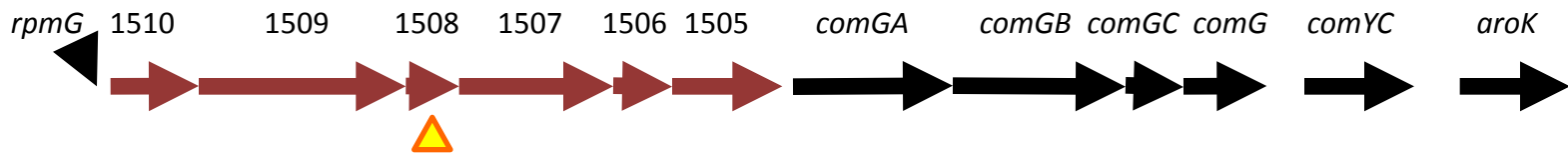
The biofilm incibility phenotype correlates with methicillin sensitivity



The bimodal dose-response curve is evidently a superposition of two biphasic dose-effect curves



Screening for induction mutants reveals novel MRSA biofilm genes



Future questions:

Why is biofilm induction specific for β -lactam antibiotics?

Do low-level β -lactam antibiotics induce biofilm *in vivo*?

Is this process clinically relevant?

Can this process contribute to the emergence of multidrug-resistant bacteria in farm animals fed subtherapeutic levels of penicillin?

Funding

