Diffusion Retardation by Buffering of Tobramycin in Alginate Biofilms

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Abstract:
The killing of bacteria by antibiotics in biofilms is known to be reduced by 100-1000 times relative to planktonic bacteria. This makes such infections difficult to treat. We suggest that a biofilm should be regarded as an independent compartment with distinct pharmacokinetics. To elucidate this, we have measured the penetration of the tobramycin into seaweed alginate beads which serve as a model of the extracellular polysaccharide matrix in *P. aeruginosa* biofilm. We find that, rather than a normal first order saturation curve, the concentration of tobramycin in the alginate beads follows a power-law as a function of the external concentration. The power-law appears to be a consequence of binding to a multitude of different binding sites. In a diffusion model these results are shown to produce pronounced retardation of the penetration of tobramycin into the biofilm. This filtering of the free tobramycin concentration inside biofilm beads is expected to aid in augmenting the survival probability of bacteria residing in the biofilm. PLOS ONE, 11, 4, e0153616, 2016.
:

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Diffusion Retardation by Binding of Tobramycin in Alginate Biofilms

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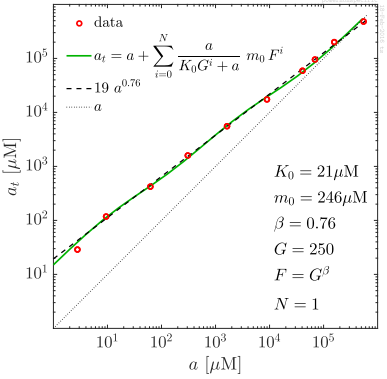
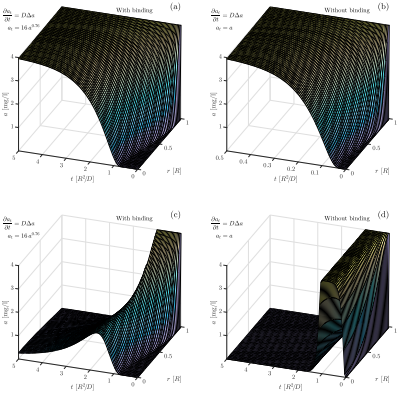
A biofilm is an independent compartment with distinct pharmacokinetics! Test: We have measured the penetration of tobramycin into alginate beads. We find that, the concentration of tobramycin in the alginate beads follows a power-law as a function of the external concentration. The power-law is a consequence of binding to multiple binding sites. The buffering results in pronounced retardation of the penetration of tobramycin into the biofilm.

Measured total concentration of Tobramycin inside alginate beads as a function of external concentration. Follows power law! Non-specific binding explains power law.



[PLoS ONE **11**, 1 (2016)]

Modeled space-time profile of free tobramycin inside an alginate bead.



[PLoS ONE **11**, 1 (2016)]

Reaction diffusion model:

$$\frac{\partial a_t}{\partial t} = D\Delta a \qquad a_t = \alpha\ a^\beta \qquad \text{“retardation”} = \alpha\beta\ a^{\beta-1}$$