MATTHEW SCOTT, University of Waterloo

Using mathematics to untangle mechanism from physiology

Bacterial growth environment strongly influences the efficacy of antibiotic treatment, and slow growth is often associated with decreased susceptibility. Focusing on ribosome-targeting antibiotics, we find that the interplay between physiology and antibiotic action is more subtle, and in fact faster growth decreases susceptibility for some antibiotics within this class. Remarkably, these observations can be explained by a simple mathematical model that combines drug transport and binding with physiological constraints. Our model reveals that growth-dependent susceptibility is controlled by a single parameter characterizing the 'reversibility' of antibiotic transport and binding. Drug action and bacterial metabolism are mechanistically complex; nevertheless this study illustrates how coarse-grained mathematical models can be used to integrate pathogen physiology into drug design and treatment strategies.