SCHOOL OF LIFE SCIENCES / FACULTE DES SCIENCES DE LA VIE

Global Health Institute / Institut de recherche en infectiologie

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

GHI Seminar

Dr. Pia zur Wiesch

Harvard University

Classic reaction kinetics can explain complex patterns of antibiotic action

Finding optimal dosing strategies for treating bacterial infections (e.g. dosing frequency, dose levels, and duration of therapy) is extremely difficult, and improving therapy requires costly and time-intensive experiments. Quantitative predictions of drug-mediated bacterial killing would enable rational design of antibiotic treatment strategies. However, this requires a better mechanistic explanation of drug effects. Three poorly understood phenomena complicate predictions of antibiotic activity: post-antibiotic growth suppression, density-dependent antibiotic effects and persister cell formation. Here, we show that chemical binding kinetics alone are sufficient to explain these three phenomena, using single-cell data and time-kill curves of *Escherichia coli* and *Vibrio cholerae* exposed to a variety of antibiotics in combination with a novel theoretical model. This work provides a parsimonious mechanistic explanation for all three phenomena. Our model reproduces existing observations, has a high predictive power across different experimental setups, and makes several testable predictions, which we were able to verify in new experiments. While a variety of biological mechanisms have previously been invoked to explain post-antibiotic growth suppression, density-dependent antibiotic effects, and especially persister cell formation, our findings reveal that a simple model which considers only binding kinetics provides a unifying explanation for these three complex, phenotypically distinct behaviours. This 'chemical reaction kinetics'-based approach should provide insight for more rapid and cheaper development of new strategies for antibiotic and other chemotherapeutic regimens.

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EPFL-SV- GHI
Station 19
CH-1015 Lausanne

Tel. +41 21 693 17 57
Adm: cecile.hayward@epfl.ch
http://ghi.epfl.ch