Inhibition of bacterial growth by antibiotics

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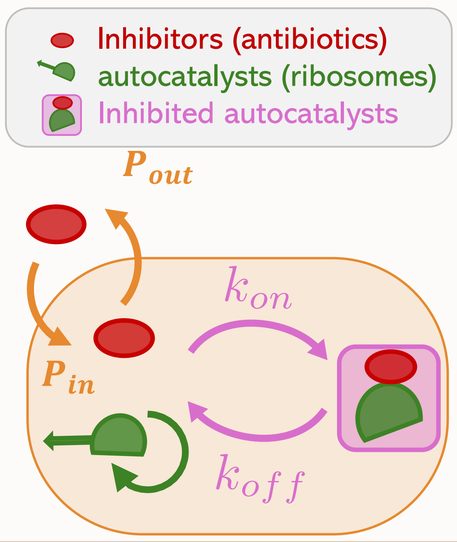
Bacteriostatic antibiotics

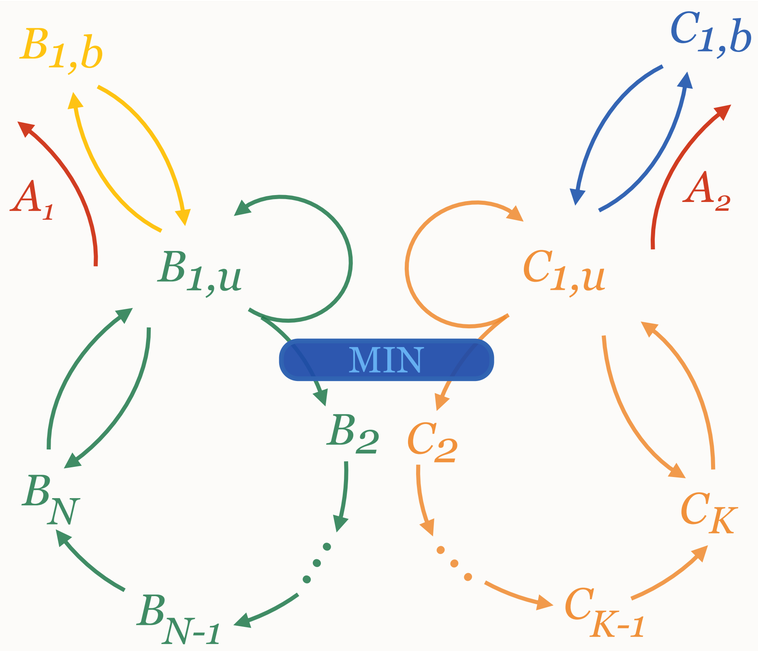


Bacteriostatic antibiotics [1] affect bacterial growth by binding to **autocatalysts** such as ribosomes, and inhibiting them.

Leontief's approach

Leontief's approach [2,3] is used to model the outcome of a supply chain where production factors have to be assembled in **fixed proportions** in order to form a product.
We use this description and work with **numbers of molecules** rather than concentrations.

Autocatalytic framework



We rely on an **autocatalytic framework** for metabolism [4], inspired from [3].

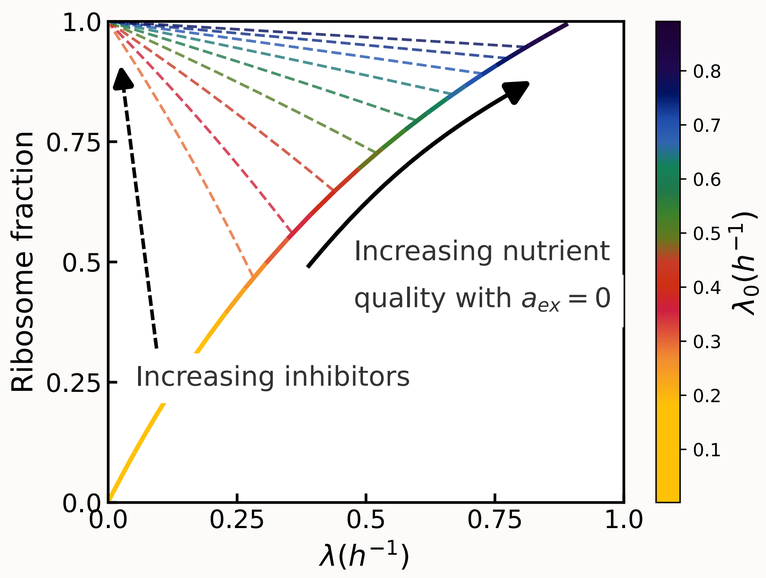
- $B_{1,u}$ is the number of unbound active ribosomes.
- $B_{1,b}$ is the number of bound ribosomes.
- A_1 is the number of antibiotics targeting

$$
\begin{aligned}
\frac{dB_{1,u}}{dt} &= k_{B3}B_3 - k_{B4}B_{1,u} - \hat{k}_{on}\frac{A}{\Omega}B_{1,u} + k_{off}B_{1,b} - \frac{B_{1,u}}{\tau_{life}} \\
\frac{dB_{1,b}}{dt} &= \hat{k}_{on}\frac{A}{\Omega}B_{1,u} - k_{off}B_{1,b} - \frac{B_{1,b}}{\tau_{life}} \\
\frac{dB_2}{dt} &= \min(k_{B1}B_{1,u}, k_{C1}C_1) - k_{B2}B_2 - \frac{B_2}{\tau_{life}} \\
\frac{dB_3}{dt} &= k_{B2}B_2 - k_{B3}B_3 + k_{B4}B_{1,u} - \frac{B_3}{\tau_{life}} \\
\frac{dA}{dt} &= P_{in}a_{ex} - P_{out}A - k_{on}\,A\,B_{1,u} + k_{off}B_{1,b} \\
&\vdots
\end{aligned}
$$

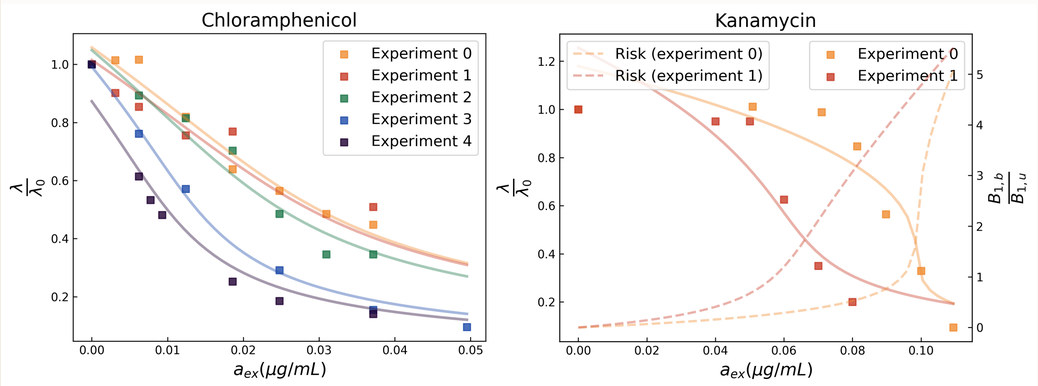
Growth laws

Two **growth laws** [5]:

- Increasing nutrient quality increases both **ribosome fraction** and **growth rate**.
- Increasing antibiotic concentration increases **ribosome fraction** while decreasing **growth rate**.



Comparison to experiments

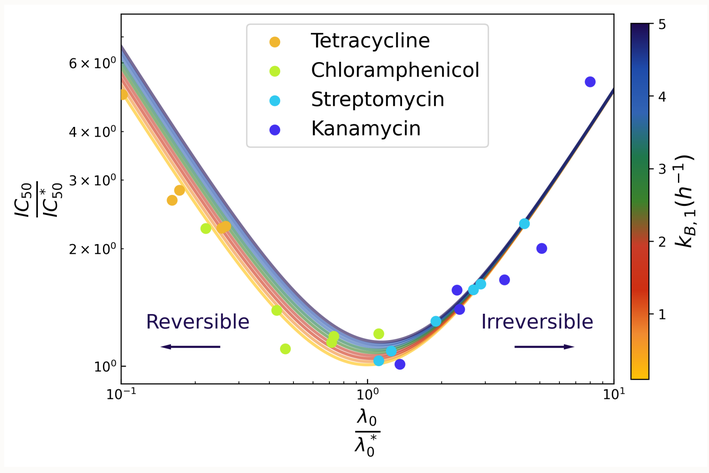


We manage to reproduce the expected decay in growth rate [5].

Reversibility

Reversible : Antibiotics unbind and leave the cell sufficiently fast [1].

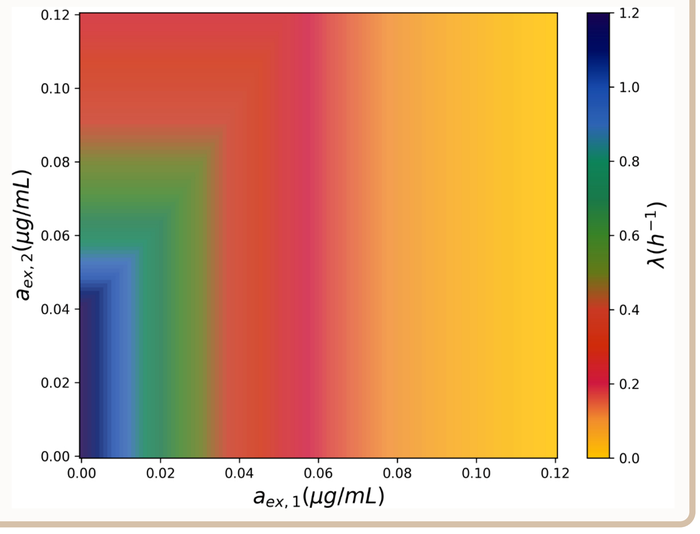
Irreversible : Antibiotics accumulate. The cell remains inhibited even if the concentration outside decreases [1].



Cumulative effects

Two antibiotics targeting different autocatalytic cycles display an **antagonistic interaction**.

Only one of them is effective at once.



[1]Greulich P, Scott M, Evans MR, Allen RJ. Molecular systems biology. 2015;11(3):796. doi:10.15252/msb.20145949.
[2]Lacoste D, Ledoux B. *Universal features of autocatalytic systems.* (2025) Economic principles in cell biology.
[3]Roy A, Goberman D, Pugatch R. PNAS. 2021;118(33):e2107829118. doi:10.1073/pnas.2107829118
[4]Ledoux B, Lacoste D. *Inhibition of bacterial growth by antibiotics : A minimal model.* (2025) arXiv:2501.02944
[5]Si F, Li D, Cox SE, Sauls JT, Azizi O, Sou C, et al. Current Biology. 2017;27(9):1278–1287. doi:10.1016/j.cub.2017.03.022.