Health Protection Research Unit in Gastrointestinal Infections at University of Liverpool

Derryk Schieck
PhD student
University of Warwick
Supervisors: Christopher Quince and Xavier Didelot

Mathematical models for transmission of antimicrobial resistance genes

Introduction

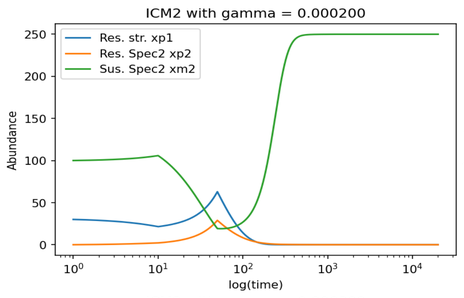
- Antimicrobial resistance (AMR) occurs when microbes develop (or gain) a defence mechanism to chemicals known as antibiotics.
- AMR is responsible for thousands of deaths each year and is expected to kill ~10 million people annually by 2050. [1]
- Mobile genetic elements such as plasmids often carry resistance genes [2] and can be transferred between certain microbes.
- We aim to understand the speed of conjugation and amount of resistance that can occur in a community.
- Can we predict abundances or composition of a microbiome after a given antibiotic has been administered. Do conjugation rates i.e. species specific factors matter?

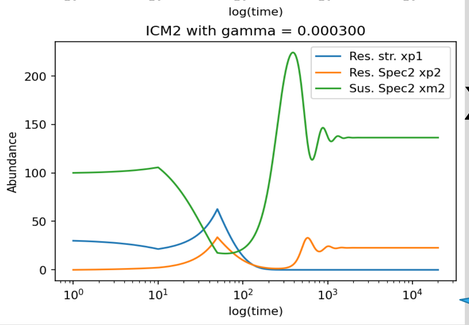
The model

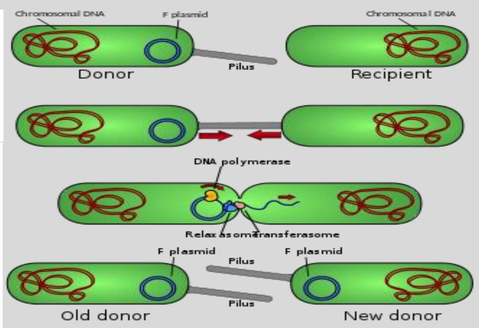
$$\frac{\mathrm{d}\vec{x}^{\pm}}{\mathrm{d}t} = \vec{x}^{\pm} \circ \left(\vec{\lambda}^{\pm} + \mathbf{A}^{\pm}\vec{x}^{\pm} + \mathbf{B}\vec{x}^{\mp}\right) \pm \vec{x}^{-} \circ \left(\mathbf{C}\vec{x}^{+}\right) + \vec{\nu}^{\pm}$$

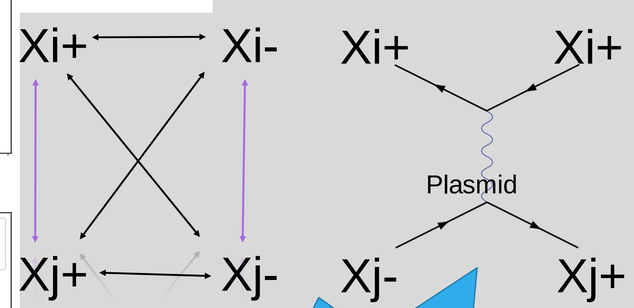
$$\gamma_{max} = \gamma_D - \frac{\sqrt{(\lambda^+\alpha^-)^2 + (\lambda^-)^2\alpha^-\alpha^+ - 2\lambda^+\lambda^-\beta\alpha^+}}{\lambda^-}$$

$$\gamma_D = \frac{\lambda^+\alpha^-}{\lambda^-} - \beta$$









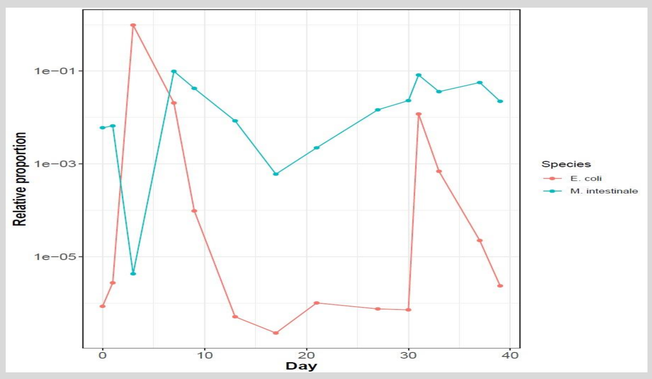
No stochastic effects!
But we observed that conjugation(especially between different species is VERY slow. This calls for a stochastic treatment. Which we work on next.

Background

- Knowledge of the underlying biological process i.e. transmission of mobile genetic elements such as plasmids.
- Ordinary Differential Equations (ODE's) are used to model the system.
- ODE's lead to dynamical systems that can show different behaviour.
- Fixed point and stability analysis shows us how the system responds to a change in a parameter.
- Do we see Hopf- bifurcations due to any of the parameters? Not yet.
- We aim to implement a stochastic version of the N-species model to account for very low conjugation rates.
- In fact: the entire conjugation process should be regarded as a stochastic process on the number of resistant individuals. Next.

Method and data

- Experiments done on gut microbiomes by sampling every other day for over a month (14 time points).
- With and without antibiotics and with and without resistance gene (plasmid).
- Use statistical inference methods such as Markov Chain Monte Carlo (MCMC) techniques to infer parameters.
- Predict outcome of microbiome species abundances after a second administration given the model described above.



References

[1] - World health statistics 2022: monitoring health for the SDGs, sustainable development goals
[2] - Evolution of horizontal transmission in antimicrobial resistance plasmids, Tatiana Dimitriu, 2022
[3] - https://commons.wikimedia.org/wiki/File:Feynman_diagram_-_Bhabha_scattering_2.svg
[4] - https://en.wikipedia.org/wiki/Bacterial_conjugation#/media/File:Conjugation.svg

The research was funded by the National Institute for Health and Care Research Health Protection Research Unit (NIHR HPRU) in Gastrointestinal Infections at University of Liverpool in partnership with the UK Health Security Agency (UKHSA), in collaboration with University of Warwick. The views expressed are those of the author(s) and not necessarily the NIHR, the Department of Health and Social Care or the UK Health Security Agency.