

University of Groningen

Evolutionary rescue theory, antibiotic resistance and the details of bacterial infection

van Eldijk, Timo; Weissing, Franz

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version

Publisher's PDF, also known as Version of record

Publication date:

2019

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

van Eldijk, T., & Weissing, F. (2019). *Evolutionary rescue theory, antibiotic resistance and the details of bacterial infection*. Poster session presented at Netherlands Society for Evolutionary Biology Meeting 2019, Ede, Netherlands.

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Does evolutionary rescue theory predict the evolution of antibiotic resistance?



Timo van Eldijk & Franjo Weissing

MARM-group, Groningen Institute for Evolutionary Life Sciences, University of Groningen, The Netherlands

For correspondence: T.J.B.van.Eldijk@rug.nl



Background & Question

When a population faces a novel (stressful) environment this may cause the population to decline. In such situations **evolutionary rescue theory** aims to predict the probability that a population adapts to the new environment (rescue), instead of facing the otherwise inevitable extinction. Thus, evolutionary rescue theory has the potential to help us understand when to expect the evolution of antibiotic resistance in bacterial populations. Yet, current models of evolutionary rescue fail to account for the mechanisms deployed by bacteria to cope with stressful conditions (like the presence of antibiotics). Here we examine two such mechanisms using stochastic modelling. First we examine the effect of **biofilm formation**, which occurs in the majority of bacterial infections. Biofilms have an explicit spatial structure, whilst standard evolutionary rescue theory assumes well-mixed populations. Secondly we examine the influence of **persister cells**, these are dormant cells that tolerate antibiotics exposure, which are also not modeled in standard evolutionary rescue theory.

How does biofilm formation and the presence of persister cells influence the probability of evolutionary rescue?

Conclusions

1. Spatial structure leads to a decreased rescue probability.
2. This is due to invading mutants locally competing mostly with themselves in spatially structured populations.
3. At high abundance (10 - 100%) the presence of persister cells increases the rescue probability.
4. However, at realistic (0 -10%) abundances persister cells do not influence the rescue probability.
5. Modelling the mechanisms that bacteria use to cope with stressful environments is important for accurately predicting antibiotic resistance.

Model biofilm

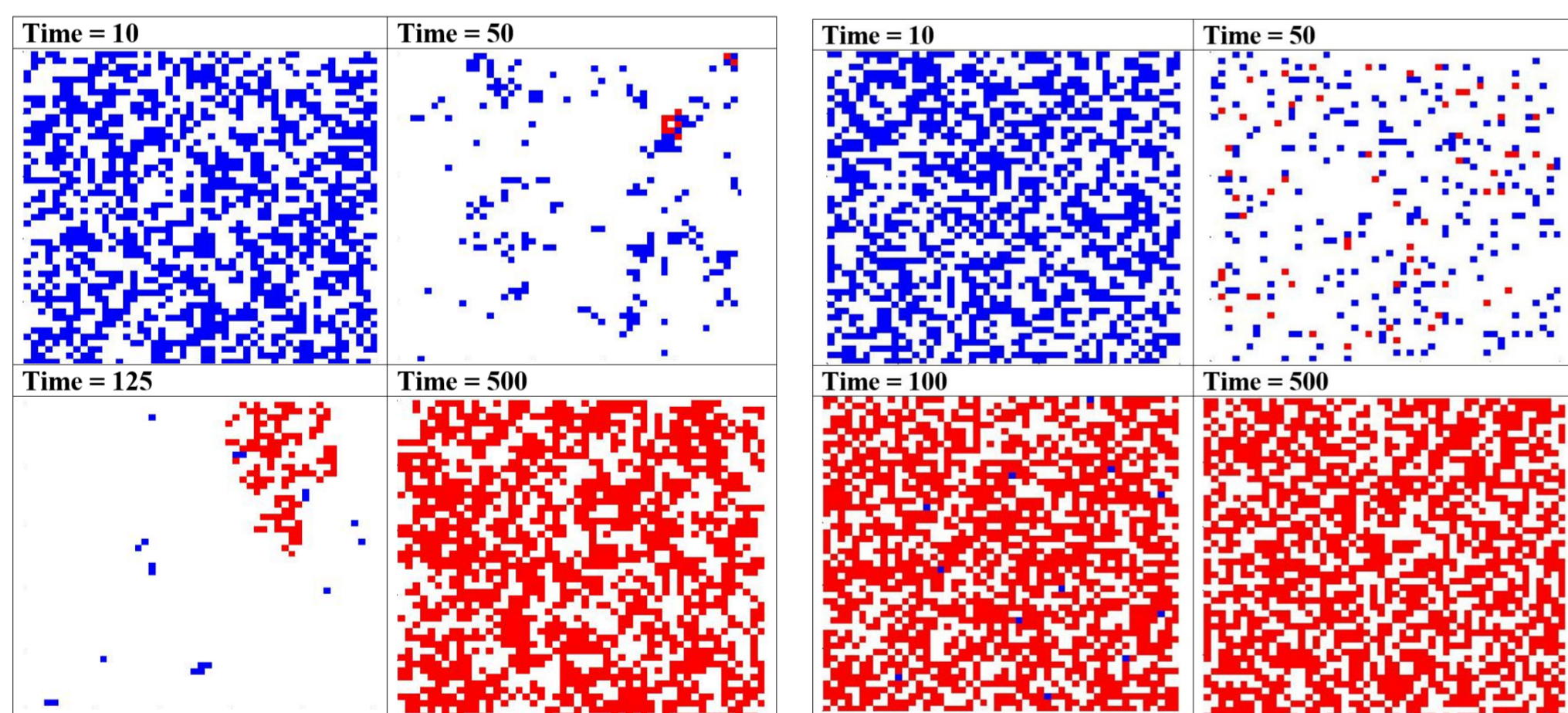
Assumptions

- Cellular automaton
- Susceptibles (negative growth rate, blue)
- Resistant (positive growth rate, red)
- Residents → Resistant (μ)
- 50 X 50 grid, initially filled with susceptibles

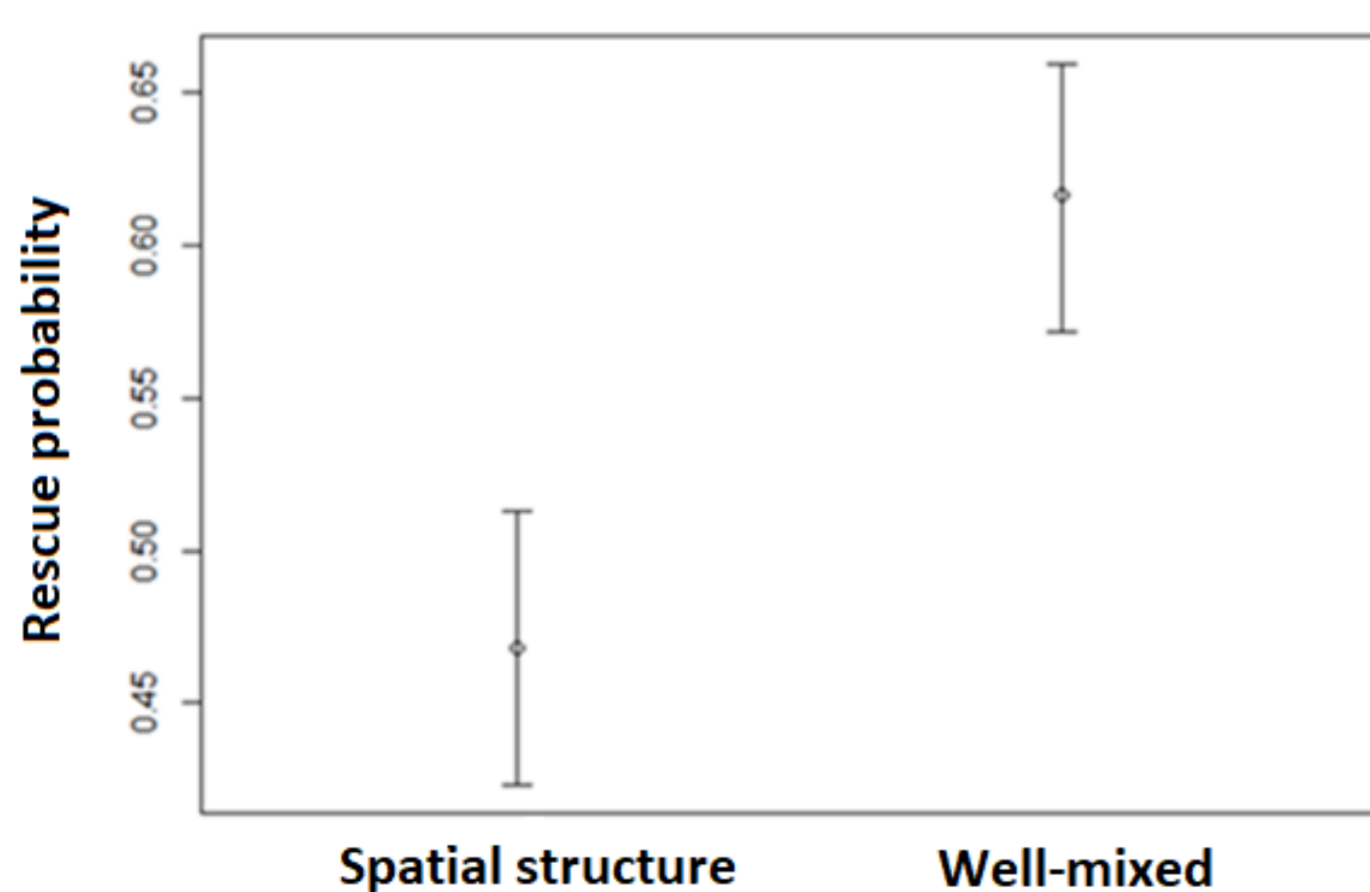
Example simulations

Spatial structure, biofilm

Well-mixed, standard rescue theory



Summary of results



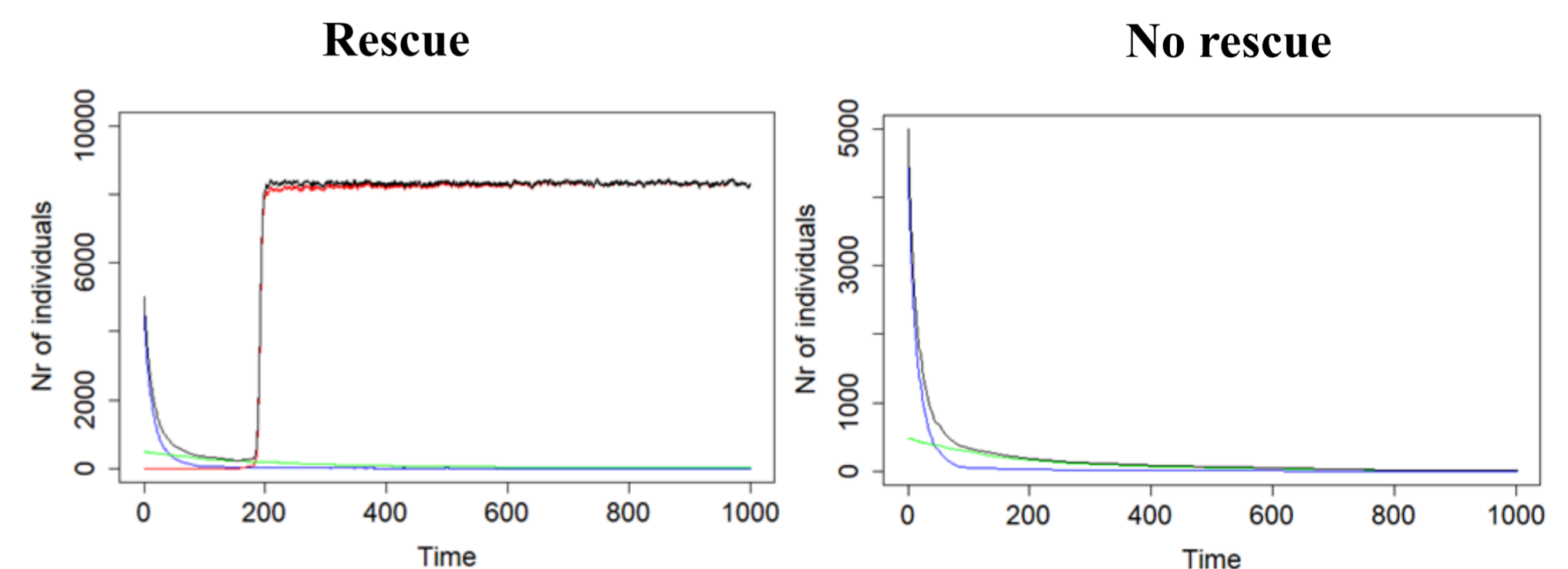
- Significant difference in rescue probability (Fisher's exact test, $p < 0.001$)

Model persister cells

Assumptions

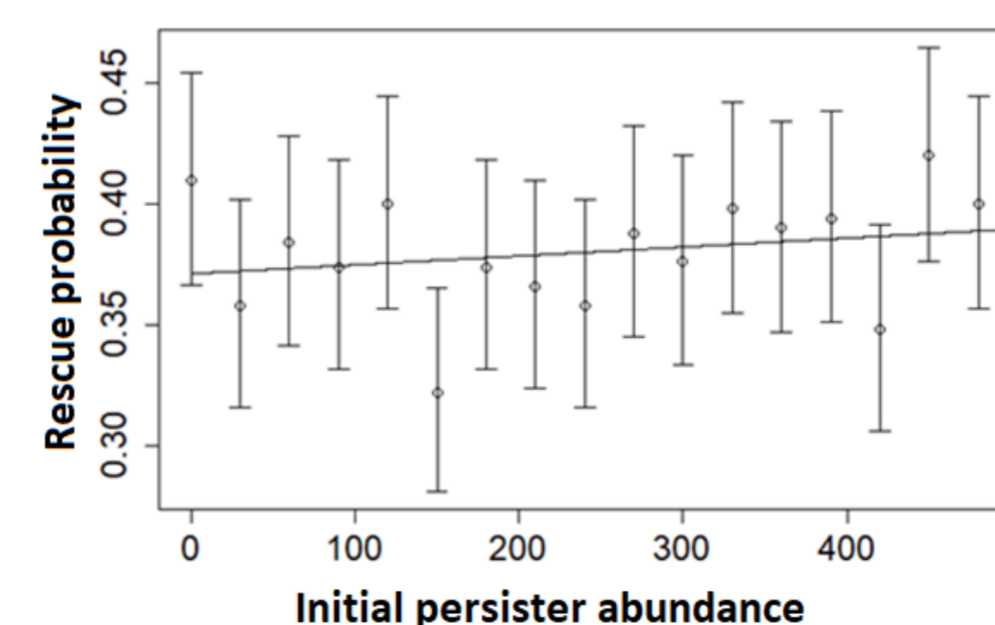
- Susceptibles (negative growth rate, blue)
- Resistant (positive growth rate, red)
- Persisters (no birth or death, green)
- Susceptibles → Persisters (P_{in})
- Susceptibles → Resistant (μ)
- Persisters → Susceptibles (P_{out})

Example simulations



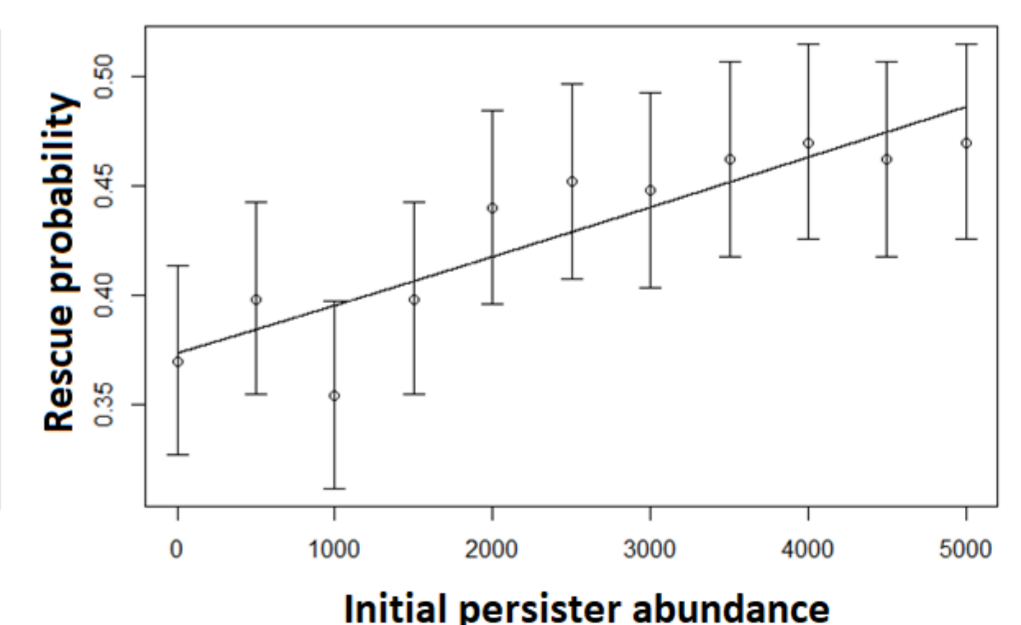
Summary of results

Realistic persister abundance (0-10%)



- No significant effect of initial persister abundance (chi-squared test $p=0.303$)

High persister abundance (10-100%)



- Significant effect of initial persister abundance (chi-squared test $p < 0.001$)