Long life of persistent cells – faults and errors resulting in a power-law decay

AUTHORS: João S. Rebelo [1] | Célia P. F. Domingues [1], Francisca Monteiro [1], Teresa Nogueira [1,2], and Francisco Dionisio [1]

[1] cE3c - Centre for Ecology, Evolution and Environmental Changes, Faculdade de Ciências, Universidade de Lisboa, 1749-016 Lisboa, Portugal

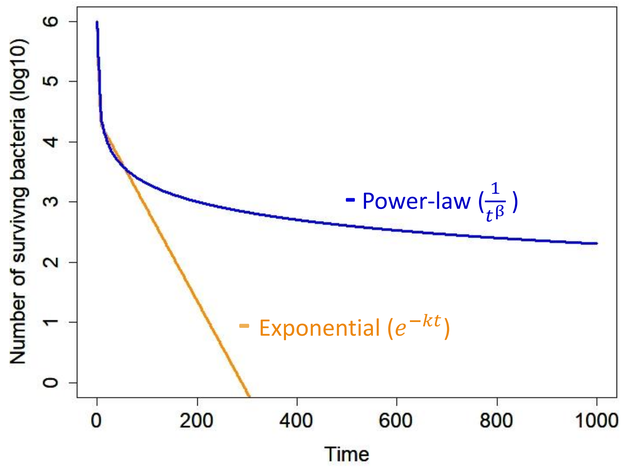
[2] INIAV, Instituto Nacional de Investigação Agrária e Veterinária, I.P. , 2780 -157 Oeiras, Portugal

R&D UNIT: cE3c

CONTACT: joaorebelo_4@hotmail.com

Introduction

Persistence is a state of bacterial dormancy where cells are phenotypically tolerant to antibiotics and other cytotoxic substances, with strong negative health impacts. There are two proposed explanations for this phenomenon: (i) several researchers have been looking for the genetic mechanism behind persistence (with the populations decaying according to an exponential) [1]; (ii) other authors argue that there is no such mechanism and that persistence results from inadvertent cell errors (with the populations decaying according to a power-law with exponent of -2) [2-4].



Methods

We simulated the survival of sensitive cells in laboratory experiments in a context of indirect resistance. Eventually, under indirect resistance, detoxifying drug-resistant cells save the persister cells which leave the dormant state and resume growth.

Conclusions

By comparing with experimental results, our simulations suggest that:

- Both exponential or power-law decays of persisters explain the experimental results
- Assuming a power-law decline, the exponent is close to the expected one if persistence results from unintentional errors

The similarity of the exponents found with two different experimental methods, with that predicted theoretically [5], suggests that the persister population indeed decays according to the power-law.

Implications

The power-law distribution has a long tail, which means that, at least theoretically, some sensitive bacteria may survive for several weeks, eventually after the end of antibiotic uptake by the patient. Long-lived persisters may lead to the failure of antibiotic treatment because some of these cells may leave the dormant state and reinitiate growth. Persistence can be a significant cause for recurrent and chronic infections.

References:

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