Revisiting the Evolution of Aging:
Repair is the Optimal Unicellular Strategy

Robert J Clegg, Rosemary J Dyson & Jan-Ulrich Kreft
Centre for Systems Biology, University of Birmingham, UK

NATURAL ENVIRONMENT RESEARCH COUNCIL

iDynoMiCS
iDynoMiCS - individual-based Dynamics of Microbial Communities Simulator

Introduction

Replicative senescence, the life strategy leading to aged parents and rejuvenated offspring, has been reported in bacteria and linked to segregation of damaged protein at division. If replicative senescence is indeed a universal phenomenon, this could have major implications for aging research and the treatment of bacterial infections (e.g. tuberculosis).
Previous mathematical models have suggested that segregating damage at division and abandoning repair leads to the highest evolutionary fitness.

Questions

We use a mathematical model of microbial aging to ask:

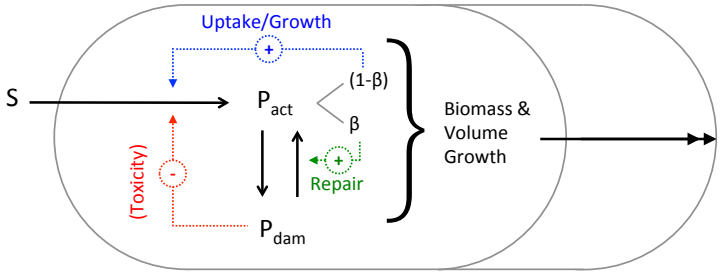
- Is replicative senescence really that beneficial?
- Should repair be abandoned when it is so common in nature?
- How well might the two aging strategies combine?

Our model is based on an established model of microbial community dynamics[1]. We tested over a wide range of parameters, in both a constant environment and a chemostat, and checked our assumptions.

Each cell is modeled individually and in terms of its protein, which is either active (P_{act}) or damaged (P_{dam}).

Active protein takes up substrate (S) and converts it into more active protein.

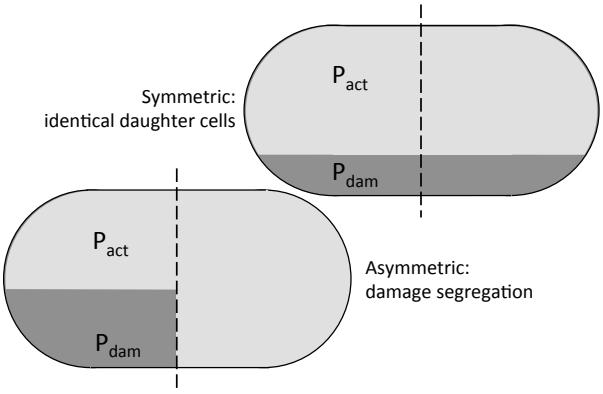
Active protein becomes damaged at a constant rate.



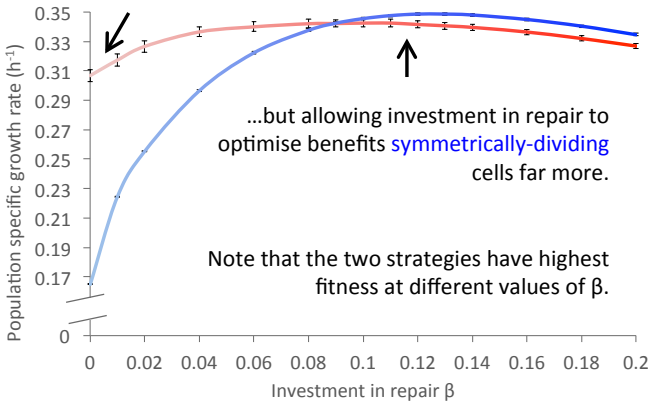
Damaged protein can be inert (simply takes up space) or toxic (hinders uptake/growth).

Investing a fraction (β) of active protein to repair is costly in two ways: growth is reduced, and repair is only 80% efficient.

Once its total protein (P_{act} + P_{dam}) reaches a threshold a cell divides and each daughter receives half the total protein.



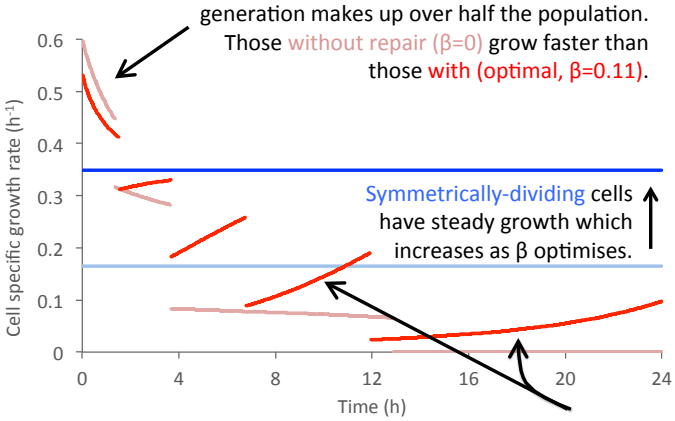
When there is no repair the asymmetrically-dividing cells are fitter…



…but allowing investment in repair to optimise benefits symmetrically-dividing cells far more.

Note that the two strategies have highest fitness at different values of β.

For asymmetrically-dividing cells the first generation makes up over half the population. Those without repair (β=0) grow faster than those with (optimal, β=0.11).



Symmetrically-dividing cells have steady growth which increases as β optimises.

The older generations benefit most from repair.

In both figures: damage accumulation rate is 0.15 h^{-1}, damage is considered toxic and substrate concentration is kept constant.

Conclusions

- Optimal investment in repair is the most important part of an aging life-strategy.
- Heterogeneity caused by segregating damage interferes with repair.
- Our model differs most from others in modeling aging as embedded within realistically-growing cells, not mere 'vehicles' for damage.
- Any replicative senescence observed is likely a side-effect (e.g. of polar growth or a swimming/attached lifestyle) and not deliberate.

Selected Reference & Contact Information

1. Lardon *et al.* (2011). iDynoMiCS: next-generation individual-based modelling of biofilms. *Environmental Microbiology* **13**:2416-2434

Email: rjc096@bham.ac.uk
Websites: www.idynomics.bham.ac.uk
www.biosciences-labs.bham.ac.uk/kreftlab/rob/