In silico evolution of bet-hedging strategies

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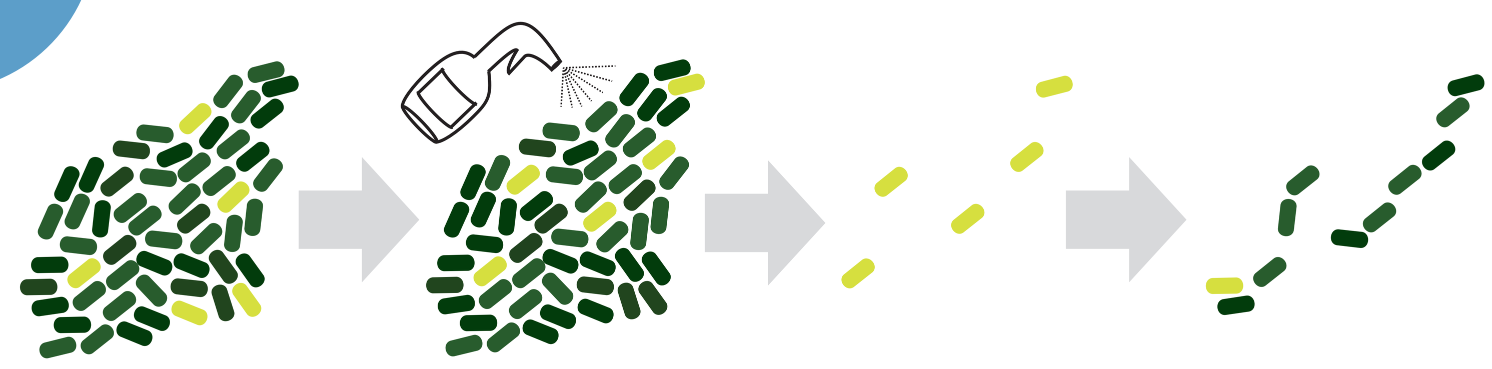
1 Introduction

Bet-hedging is an effective population level survival strategy in which a small subpopulation of cells anticipate a catastrophic event, depicted in figure 1. An important example is the phenotypic resistance to antibiotic application in persister cells of *Escherichia coli* [1].

We wish to characterise environmental regimes and network topologies that give rise to bet-hedging behaviours. We use in silico evolution of boolean network models under variable simulated environmental conditions.

2 Figure 1: Bet-hedging



After antibiotic application, a phenotypically resistant sub-population (pale green cells) survive, and the population continues to grow when the antibiotic is taken away.

3 Approach

1. Initialise random boolean networks (figure 2)
2. Calculate fitness according to figure 3
3. Perform mutations and recombination
4. Evolve the system: repeat steps 2 – 3

To ensure our boolean framework allows sophisticated behaviours necessary for bet-hedging, we attempt to reproduce previous network evolution results [2] by evolving clocks under a variable environment.

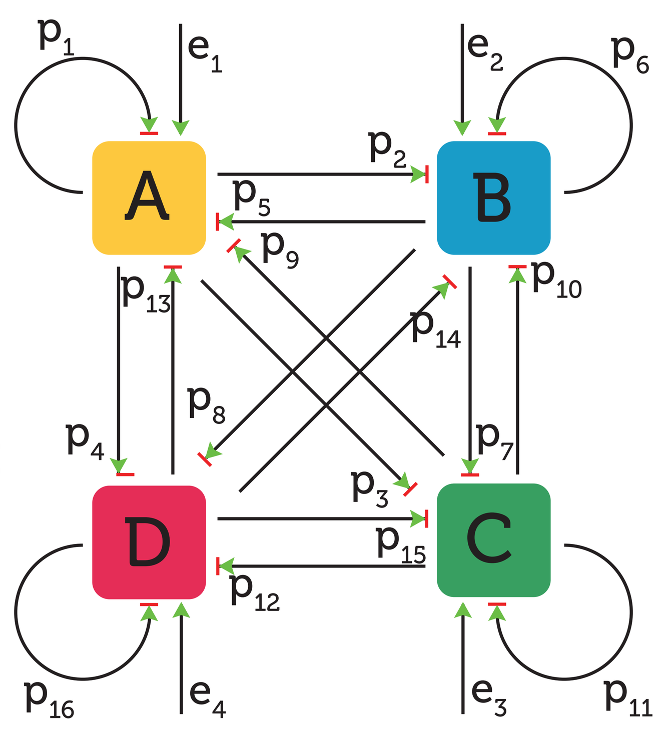
4 Figure 2: General network topology

paths are randomly assigned:

- activation or repression
- time delay (5 < minutes < 60)

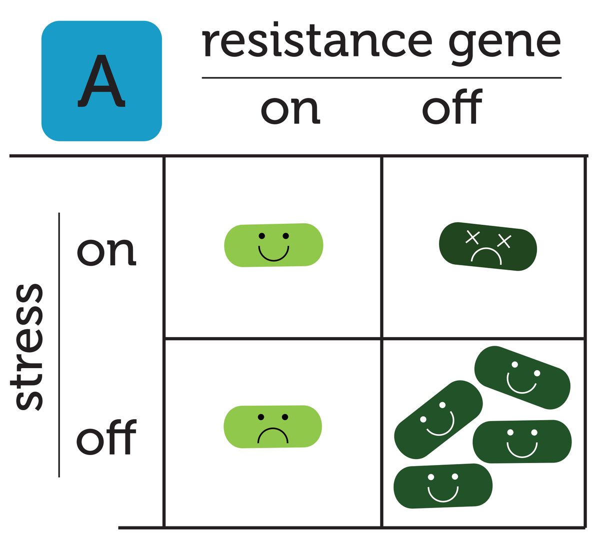
genes are randomly assigned:

- environmental sensing
- logic gate (and / or)



5 Figure 3: Fitness functions for evolving bet-hedging and clocks

A. Bet-hedging



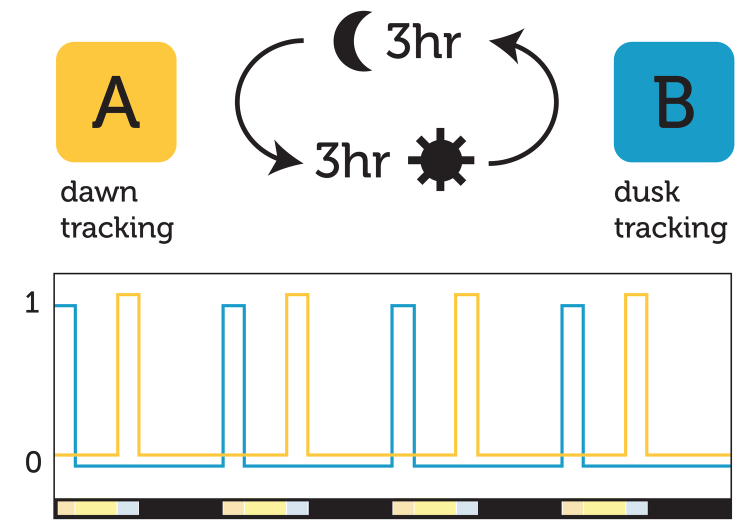
A. Bet-hedging

- simulated antibiotic resistance
- cells expressing the resistance gene cannot reproduce
- cells not expressing resistance gene during random antibiotic applications will die

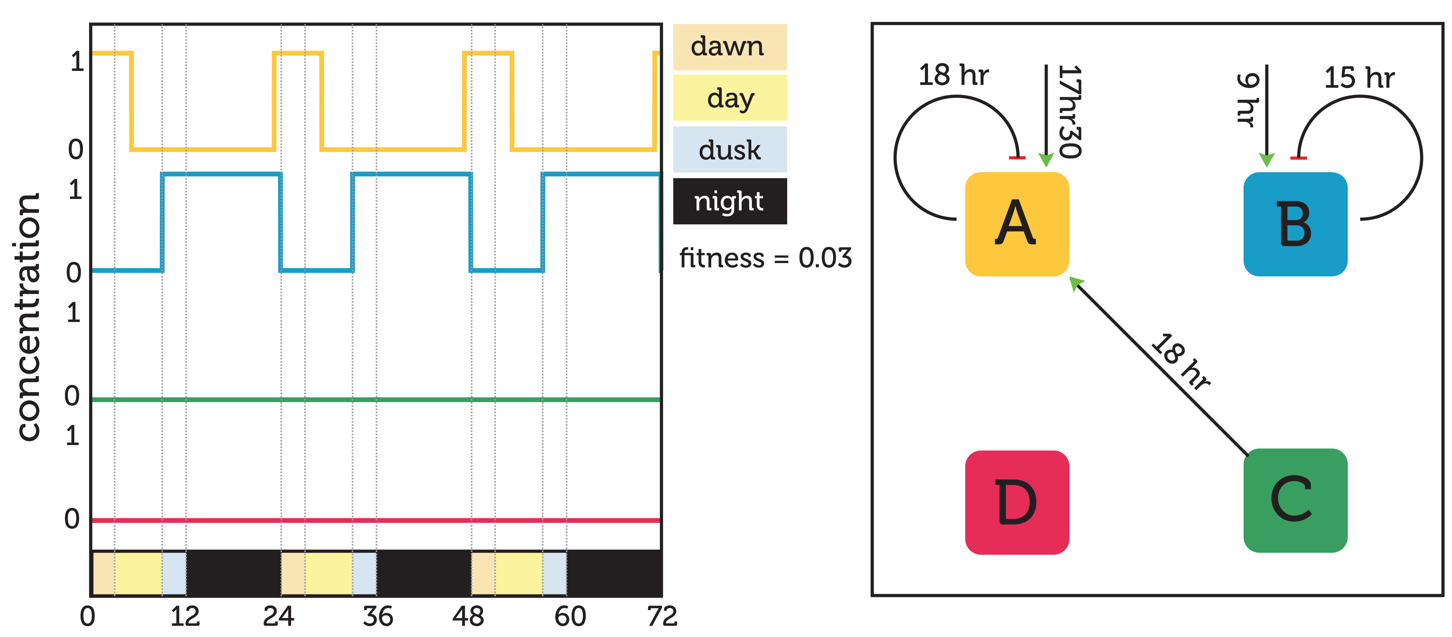
B. Clock

- networks that can track dawn and dusk accurately

B. Clock



6 Figure 5: Evolved clock network



Simulation traces on the left show that gene A tracks dawn and gene B tracks dusk imperfectly. The network topology is simple so fitness may be stuck in a local maximum.

7 Conclusions and further work

- simple boolean networks can evolve into clocks
- genetic algorithm needs optimising for faster convergence
- next will add noise to the environmental light/dark cycles
- then will implement bet-hedging fitness function

8

[1] Rotem, E., et al. (2010), PNAS 107 (28), 12541–12546.

[2] Troein, C., Locke, J. C. W., et al. (2009), Current Biology 19, 1961–1964.

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