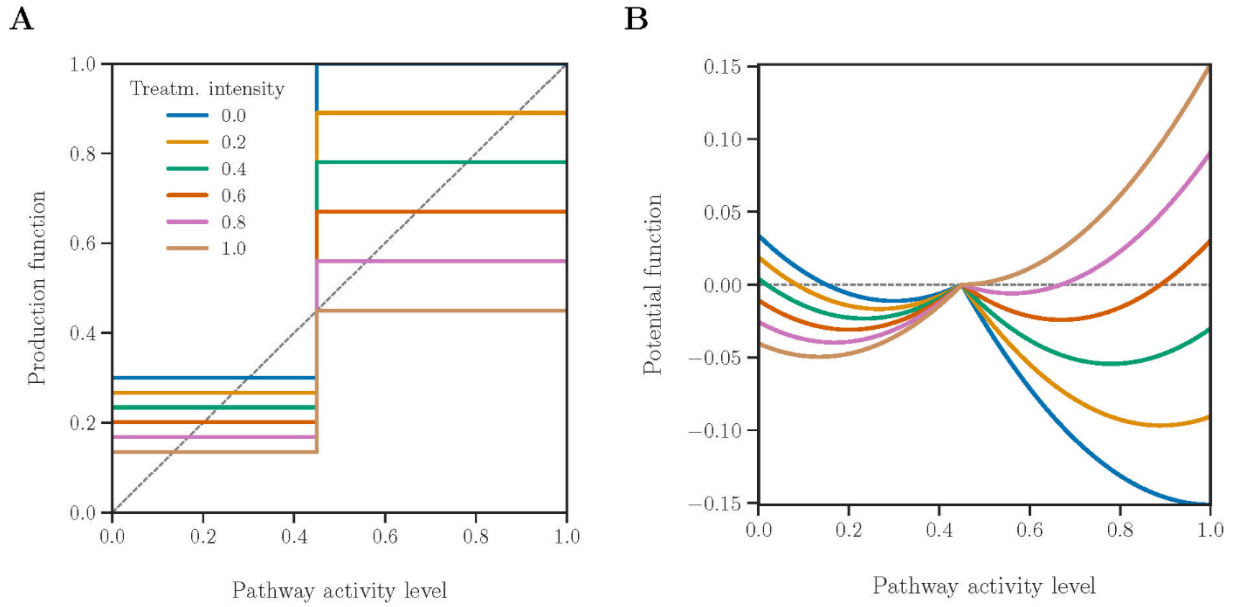


1 **Supplementary figures**

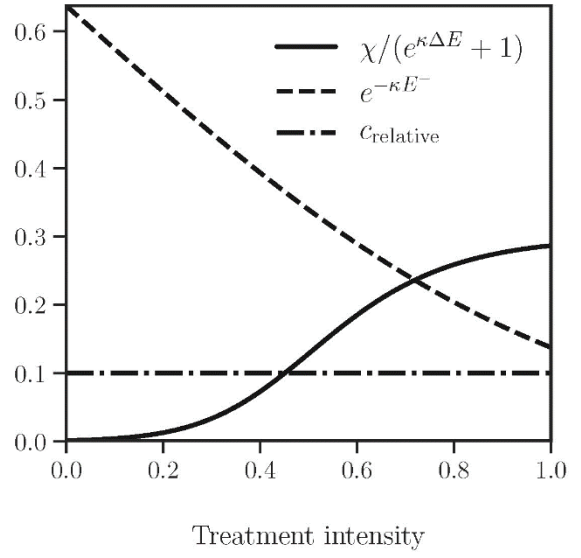
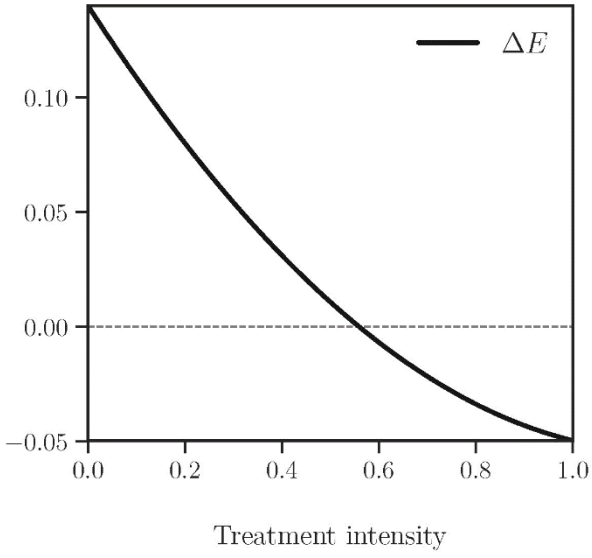
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3

4 **Fig S1: Production function (A) and corresponding set of potentials (B) under varied**
5 **treatment intensities.** The grey dashed in B indicates the zero level in the potential.

6

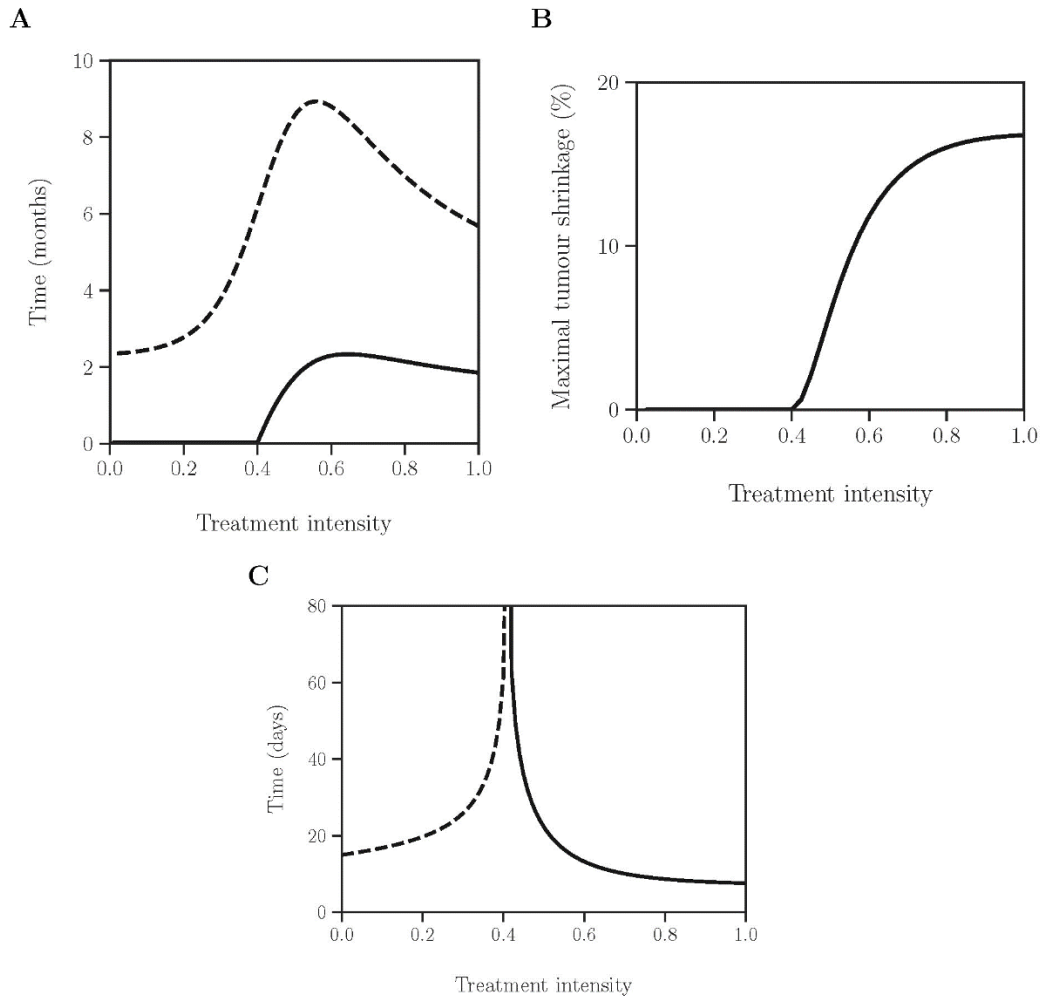


1

2 **Fig S2: Main characteristics of the equations (5)–(6) as the functions of treatment intensity.**

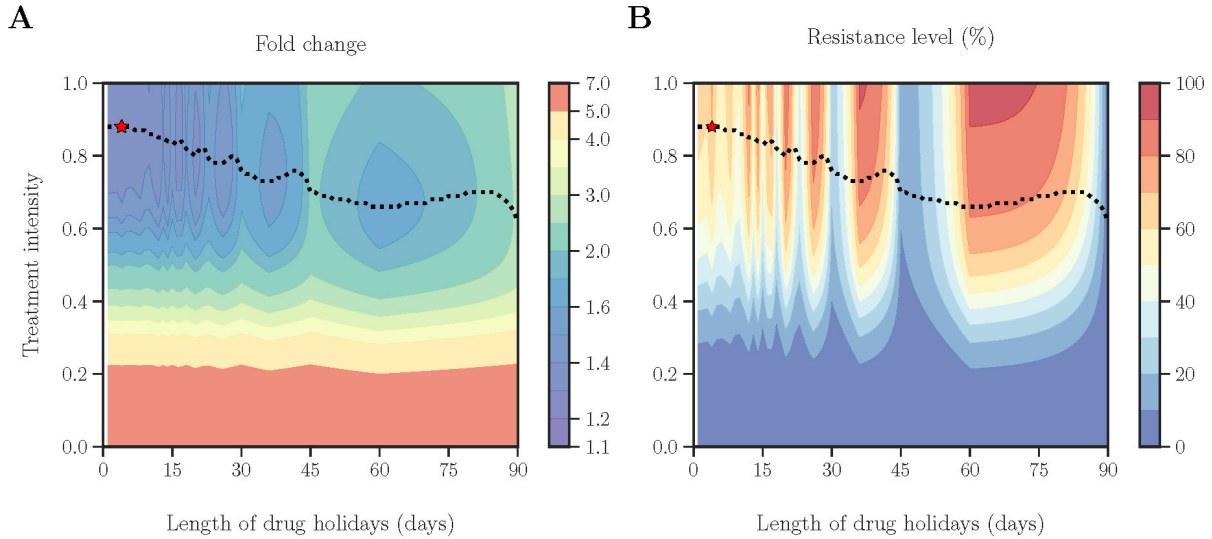
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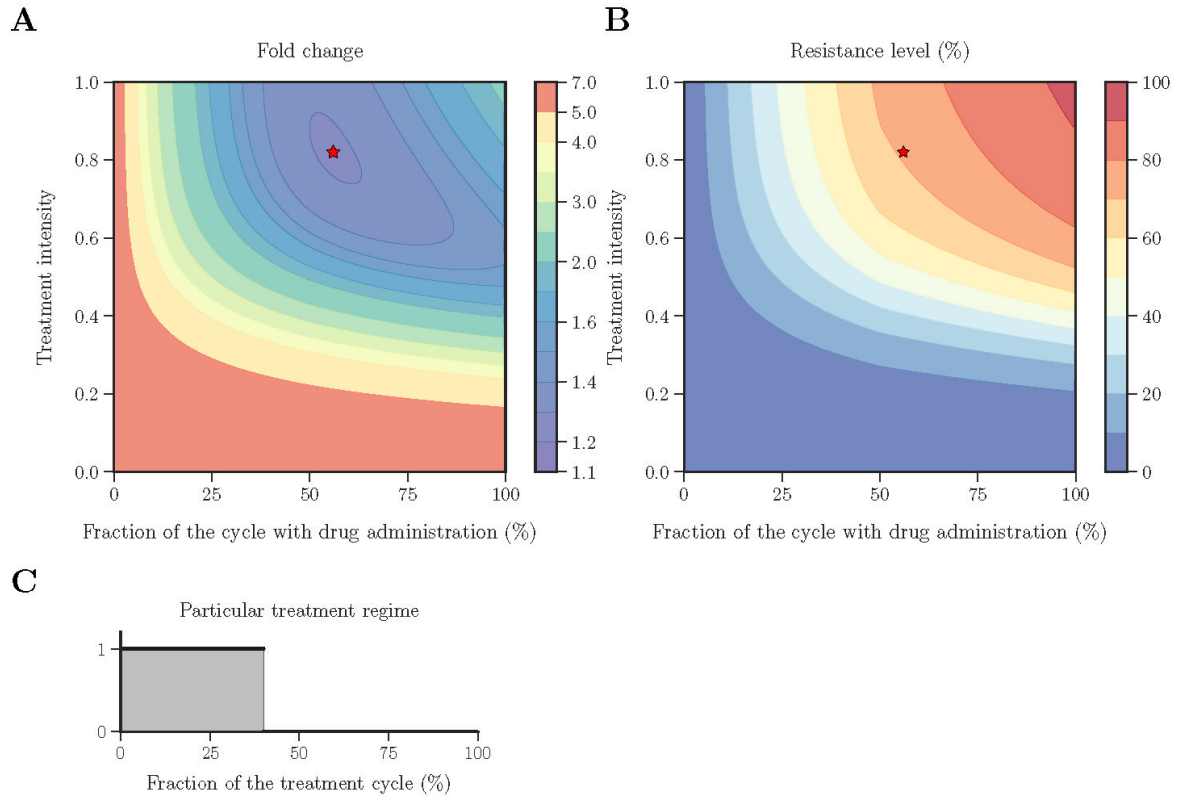
4 **Fig S3:** (A) Relapse times of returning to the initial size for tumours under static treatments (the
5 solid line). For comparison, the dashed line indicates the time necessary for a two-fold increase in
6 size. (B) Maximal tumour shrinkage observed during the static treatment. (C) Time necessary to
7 acquire 50%-level of resistance starting from the initial 0% (solid) vs. the time necessary to lower
8 the resistance level from the initial 100% to 50% (dashed) under the static treatment regimen.



1

2 **Fig S4: Analysis of periodic treatment regimen with equal durations of active phases and**
 3 **drug holidays.** The fold change in tumour size after six months of treatment (A), and the final
 4 resistance level within a tumour (B) are characterized by repeating patterns. A line of dots
 5 represents the minima in fold change for fixed length of active phases/drug holidays and varied
 6 average treatment intensity. The red star indicates the global minimum.

7

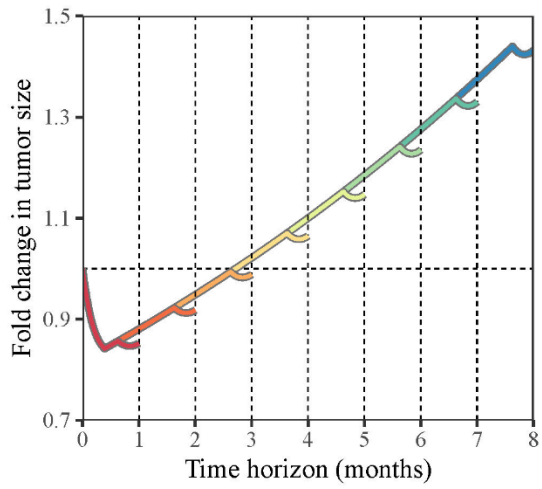


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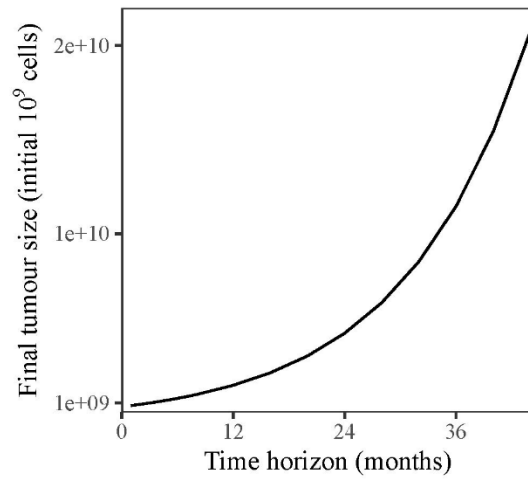
2 **Fig S5: Outcomes of the periodic treatment with 8-day periods of varying duty cycles (ratio**
 3 **of the active phase duration to the duration of the period): fold change in tumour size (A),**
 4 **final resistance level (B).** (C) illustrates the asymmetry in the treatment schedule and the applied
 5 treatment intensity during the active phase.

6

A



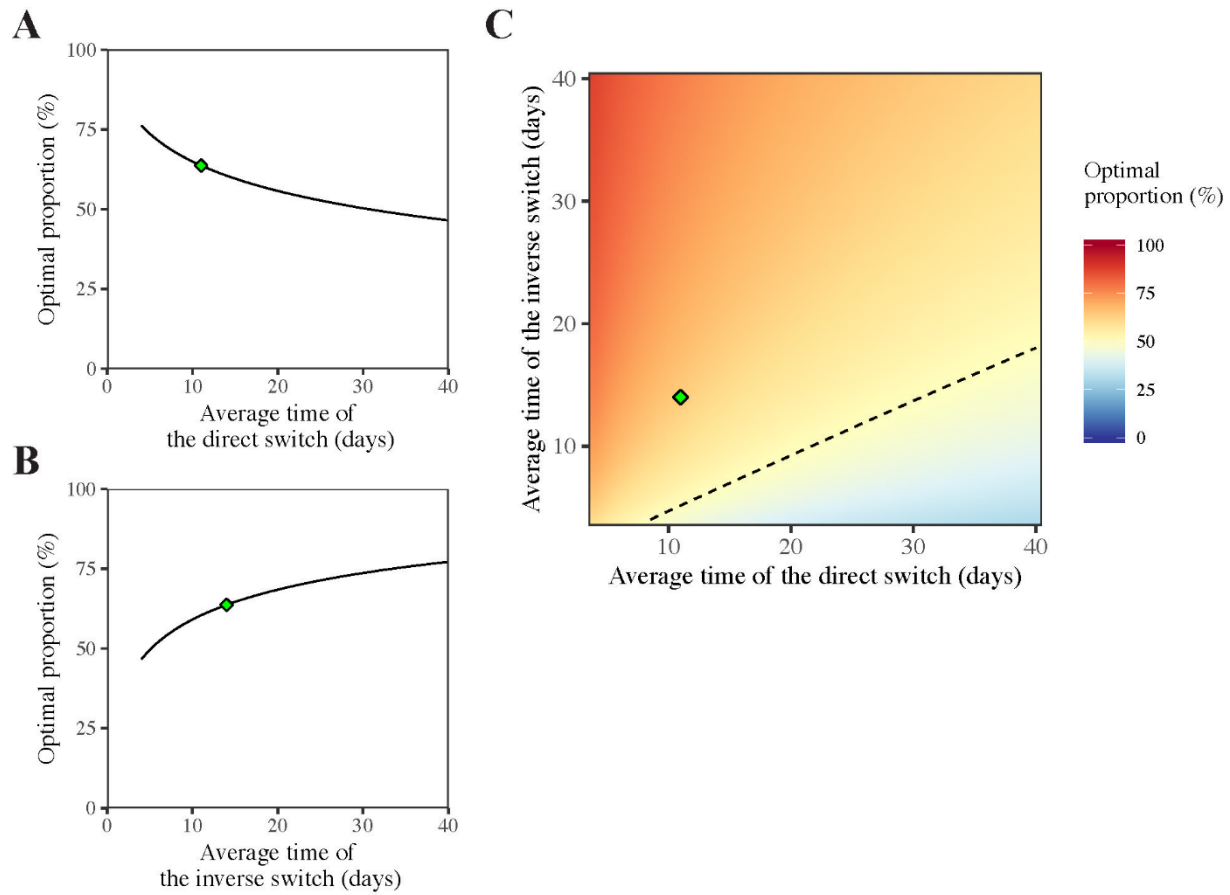
B



1

2 **Fig S6: (A)** Realization of optimal treatments with different terminal times. **(B)** Tumour sizes at
3 the termination of the optimal treatment schedule.

4



1

2 **Fig S7: Optimal balance between sensitive and resistant cells as a result of optimal problem.**

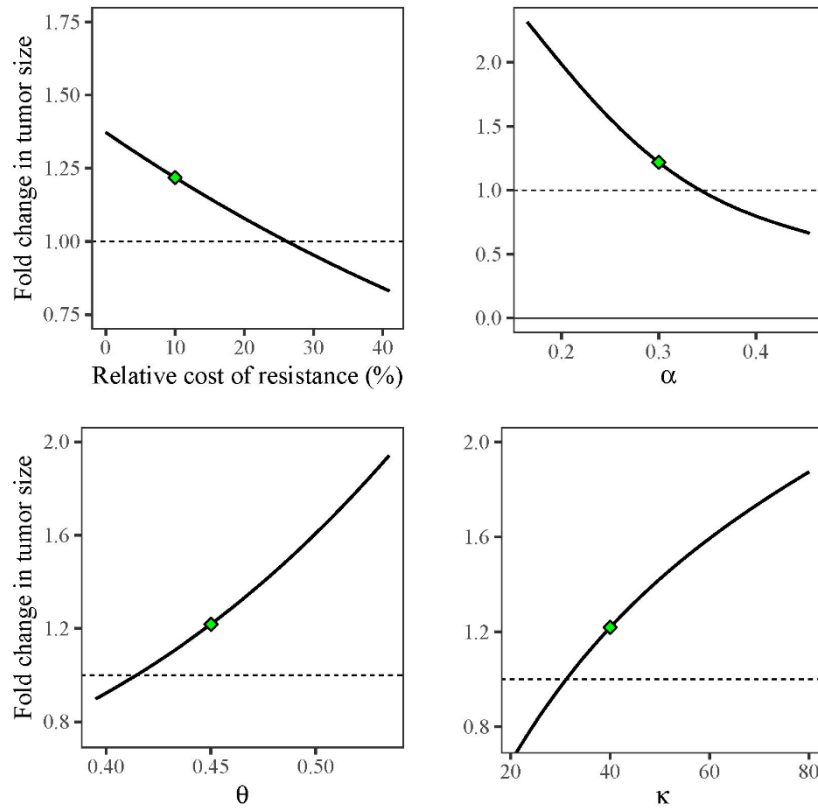
3 (AB) The change in optimal proportion when one of switching rate is fixed at its baseline value

4 (Table 1). (C) Variation in optimal proportion for varied characteristic times. Dashed line indicates

5 the optimal proportion at 50%.

6

1



2

3 **Fig S8: Effects of single parameter values on the optimal outcome of the six months**
4 **treatment.** Other parameters remain fixed according to Table 1. The baseline parameters set and
5 the corresponding outcome are shown as green points. The fold-change of level one is shown by
6 dashed horizontal lines.

7