

A mathematical model for cancer dynamics with treatment and saboteur bacteria

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1. New model construction

A recent biological discovery is that some bacteria can metabolize the chemotherapeutic drug, sabotaging the treatment this way. Then the cancer treatment can be combined with antibiotic treatment, to remove the saboteur bacteria. We constructed a novel dynamical model of this phenomenon.

$$\begin{aligned} \text{Tumour cells:} & T'(t) = r_T T(t) (K_T - T(t)) - \delta T(t) C(t) \\ \text{Chemotherapeutic drug:} & C'(t) = \gamma - \mu C(t) - \lambda C(t) B(t) \\ \text{Bacterium population:} & B'(t) = r_B B(t) (K_B - B(t)) - \theta B(t) A(t) \\ \text{Antibiotics:} & A'(t) = \alpha - \sigma A(t) \end{aligned}$$

Control parameters:

γ : dose of the chemotherapy
 α : dose of the antibiotics

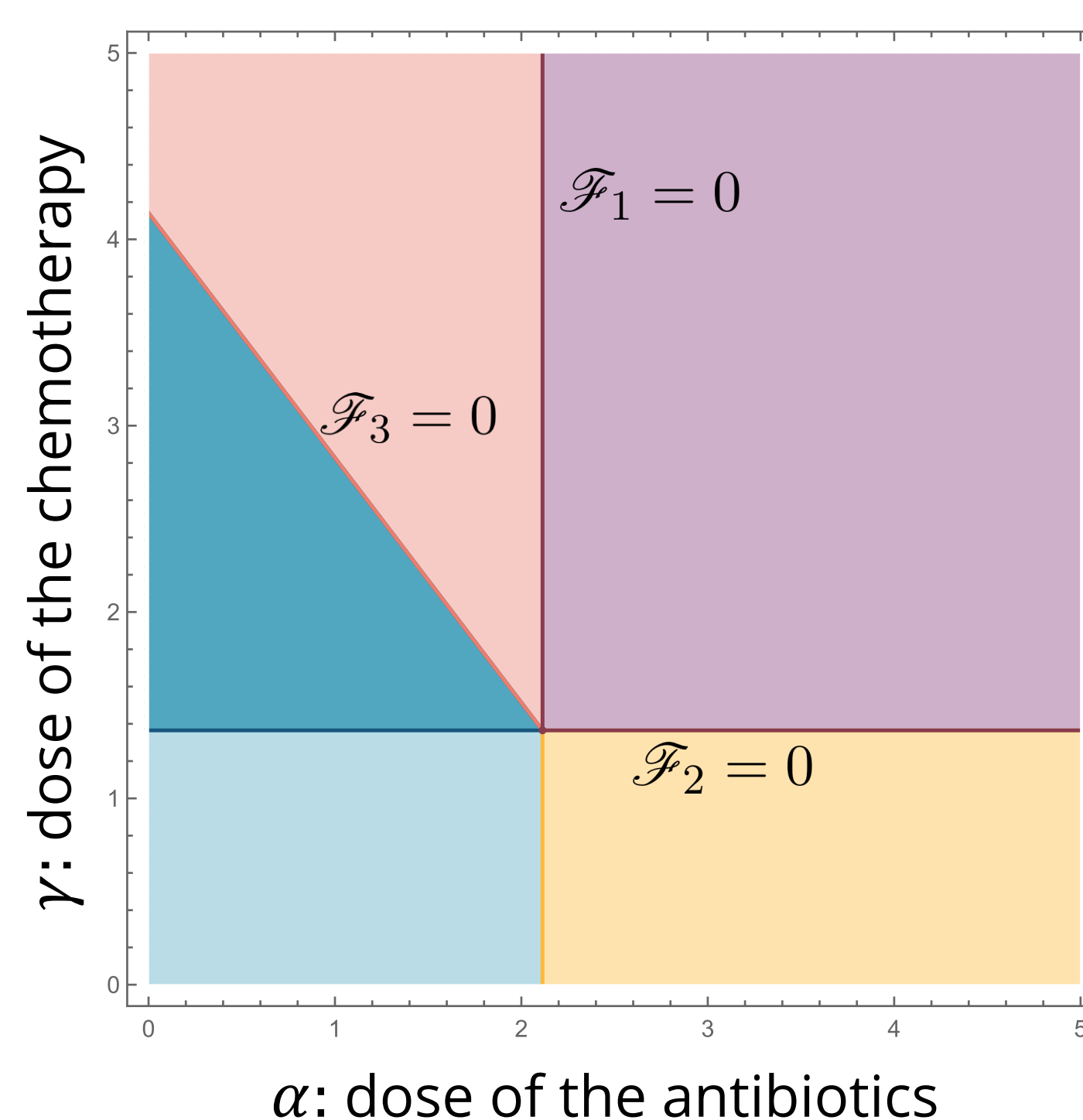
2. Threshold parameters and equilibria

Combined threshold parameters:

$$\mathcal{F}_1 = \frac{K_B \sigma r_B}{\theta} - \alpha, \quad \mathcal{F}_2 = \frac{K_T \mu r_T}{\delta} - \gamma, \\ \mathcal{F}_3 = \frac{K_T \left(\mu + \lambda \left(K_B - \frac{\theta \alpha}{\sigma r_B} \right) \right) r_T}{\delta} - \gamma$$

Types of equilibria:

- E_0 : trivial eq. ($T = B = 0$)
- E_T : tumour-free eq. ($T = 0, B > 0$)
- E_B : bacterium-free eq. ($T > 0, B = 0$)
- E_{coex} : coexisting eq. ($T, B > 0$)



The signs of the threshold parameters characterize which equilibria exist on the given domain.

Case 1 a)
 $\mathcal{F}_1 > 0, \mathcal{F}_2 > 0, \mathcal{F}_3 > 0$
 $E_0, E_B, E_T, E_{\text{coex}}$

Case 1 b)
 $\mathcal{F}_1 > 0, \mathcal{F}_2 \leq 0, \mathcal{F}_3 > 0$
 $E_0, E_T, E_{\text{coex}}$

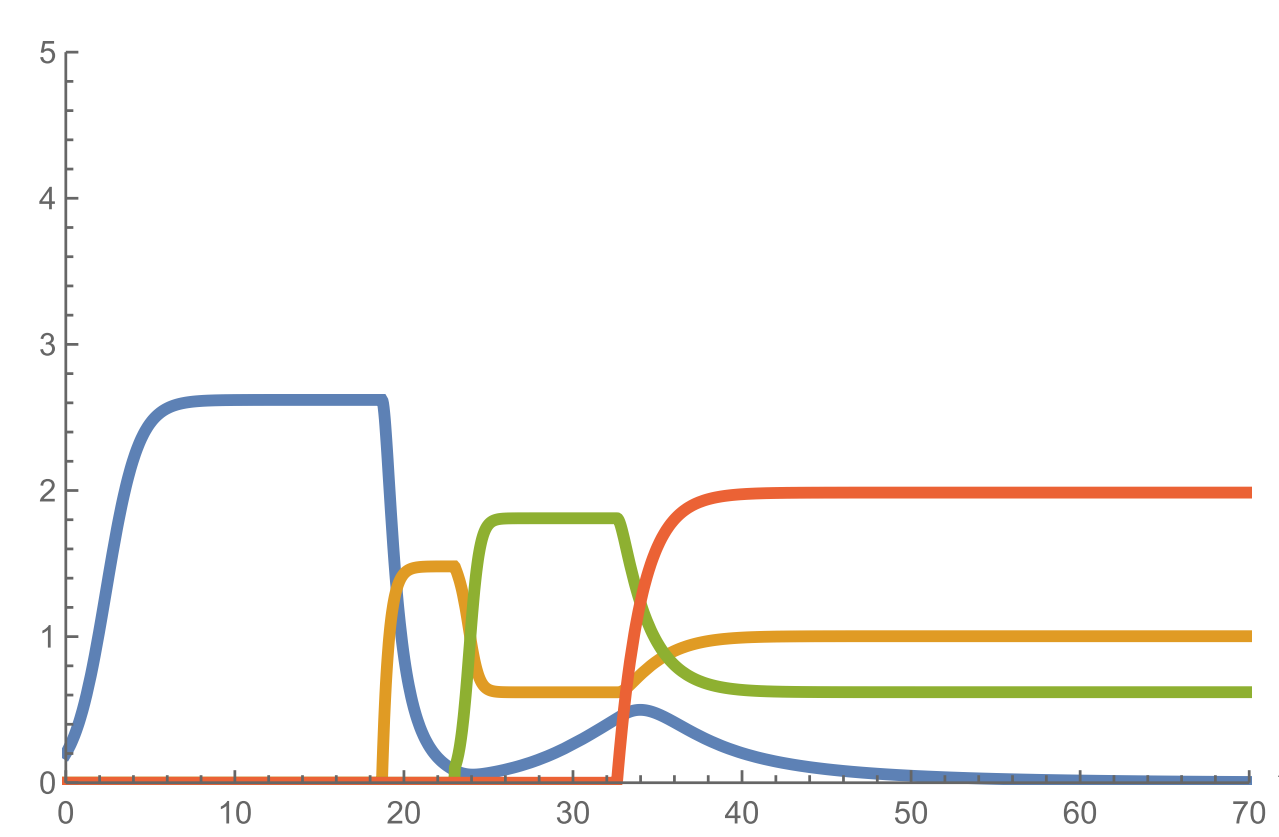
Case 2
 $\mathcal{F}_1 > 0, \mathcal{F}_3 \leq 0$
 E_0, E_T

Case 3
 $\mathcal{F}_1 \leq 0, \mathcal{F}_2 > 0$
 E_0, E_B

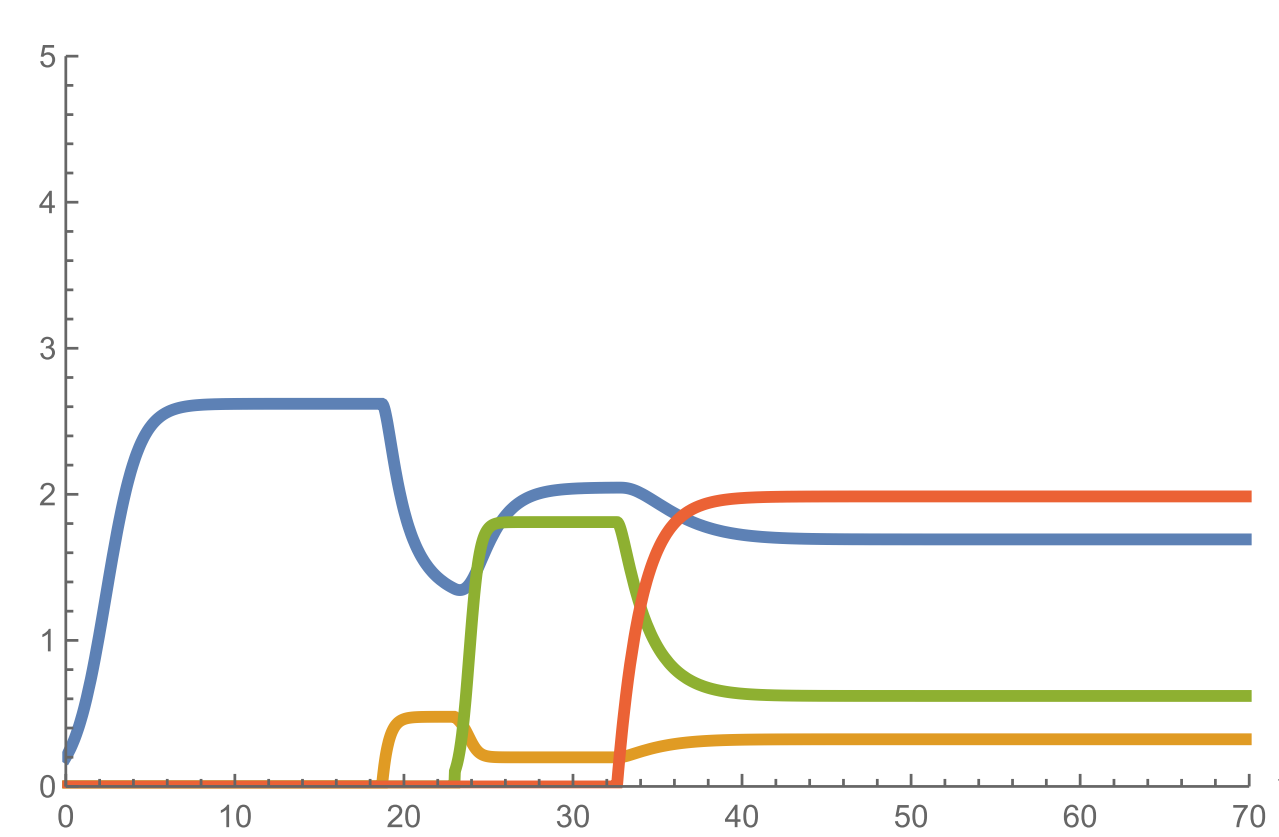
Case 4
 $\mathcal{F}_1 \leq 0, \mathcal{F}_2 \leq 0$
 E_0

Simulations

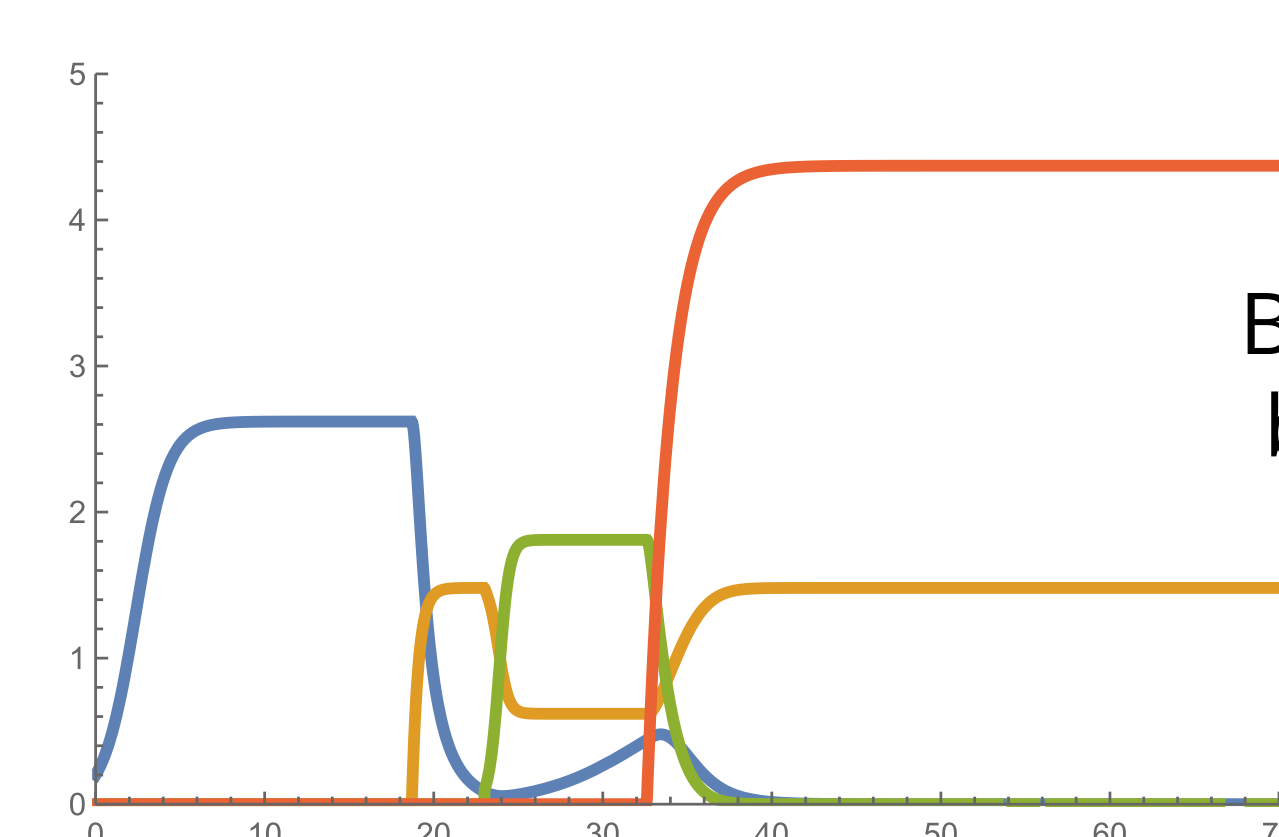
Case 2:
The tumour is eliminated,
but the bacteria survive.



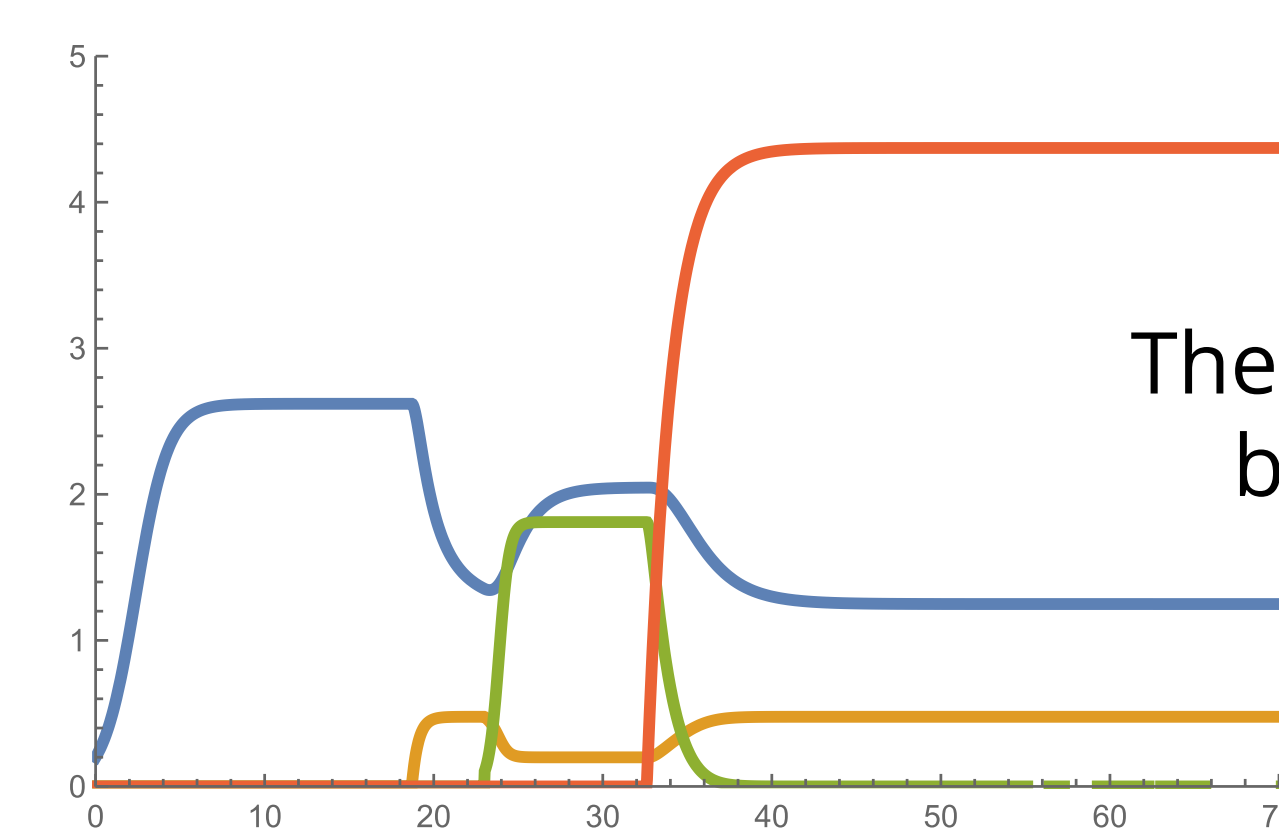
Case 1:
Both the tumour and
the bacteria survive.



Case 4:
Both the tumour and the
bacteria are eliminated.



Case 3:
The tumour survives, but the
bacteria are eliminated.



3. Global asymptotic stability

In each case, there exists exactly one globally asymptotically stable equilibria, which is

- E_{coex} in Case 1,
- E_T in Case 2,
- E_B in Case 3,
- E_0 in Case 4.

So in each case, the solutions always converge to the corresponding equilibrium. This means that we can always explicitly determine the outcome of the treatment based on the signs of the threshold parameters. The proof is based on an iterative application of a comparison principle.

4. Data fitting

We fitted a slightly modified version of our model to experimental data: the growth of colon cancer in mice in the presence of saboteur bacteria.

