Exercise 2: Frequency dependent fitness

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Experiments

Tumor-Stroma Interactions

- **Title:** Evolutionary Dynamics of Tumor-Stroma Interactions in Multiple Myeloma.
- **Authors:** Javad Salimi Sartakhti, Mohammad Hossein Manshaei, Soroosh Bateni, Marco Archetti.
- Cancer cells and stromal cells cooperate by exchanging diffusible factors.
    - Frequency-dependent selection that can be studied in the framework of evolutionary game theory.

Tumour-Stroma Interactions: payoff functions

- There are n phenotypes in a population denoted by $\{P_1, \ldots, P_n\}$.
- Each phenotype can produce one diffusible factor $\{G_1, \ldots, G_n\}$.
- Each diffusible factor j has a different effect $r_{i,j}$ on the other phenotypes i.
- The cost for P_i for growth factor G_i is denoted as c_i.
- M is the number of cells within the diffusion range.
  - There are M_j individuals of type P_j among the other group members.
- The payoff for strategy P_j is:

$$\pi_{P_j}(M_1, \ldots, M_n) = \frac{(M_j + 1) \times c_j}{M} r_{j,j} + \sum_{i=1, i \neq j}^{n} \frac{M_i \times c_i}{M} r_{j,i} - c_j \ .$$

Tumour-Stroma Interactions: dynamics

- Malignant plasma cells.
- Osteoblasts.
- Osteoclasts.
- Growth factors:
  - Autocrine effects.
  - Paracrine effects.

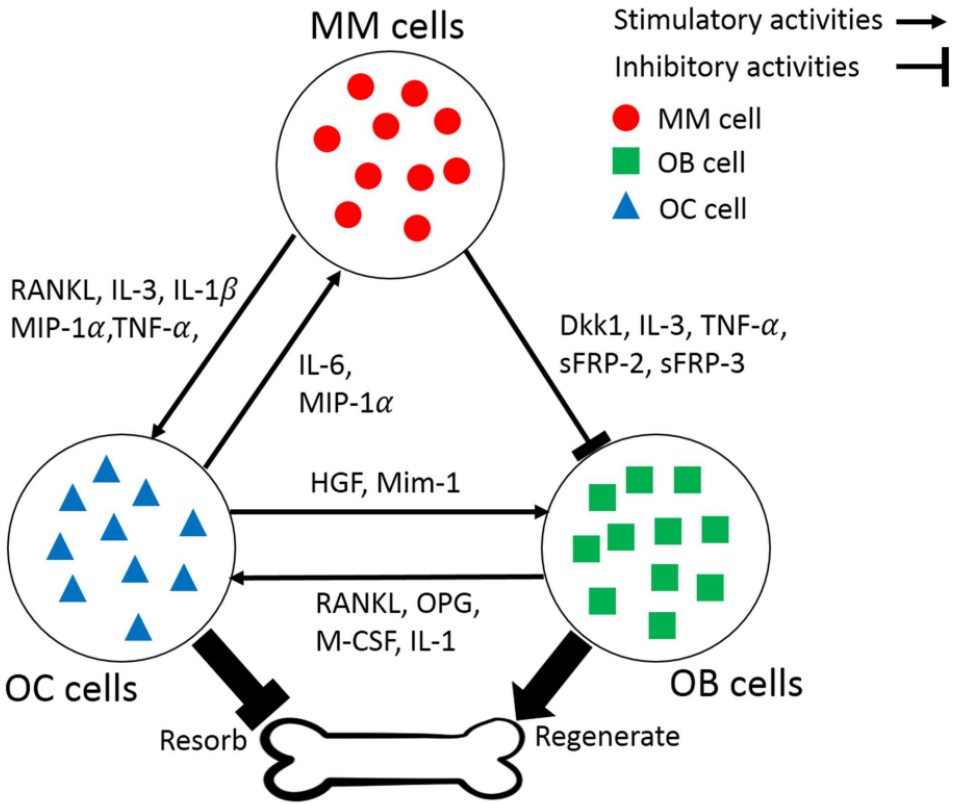

Fig 1. Bone remodeling in multiple myeloma. Multiple myeloma cells (MM) produce growth factors that activate osteoclasts (OC), which increase bone resorption, or that inhibit osteoblast (OB) differentiation. OC and OB secrete growth factors that affect each other and MM cells.

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Tumour-Stroma Interactions: Scenario 1

- $c_1 < c_2 < c_3$ (a common occurrence in multiple myeloma).
- In the presence of a small number of MM cells, the stable point on the OB-OC border becomes a saddle point and clonal selection leads to a stable coexistence of OC and MM cells.

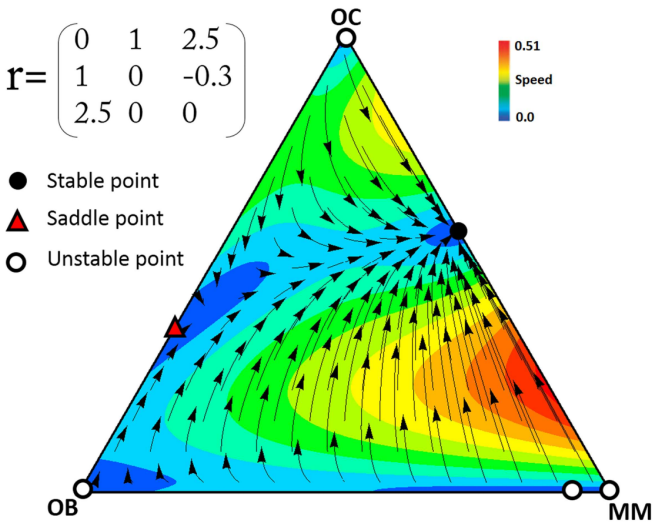
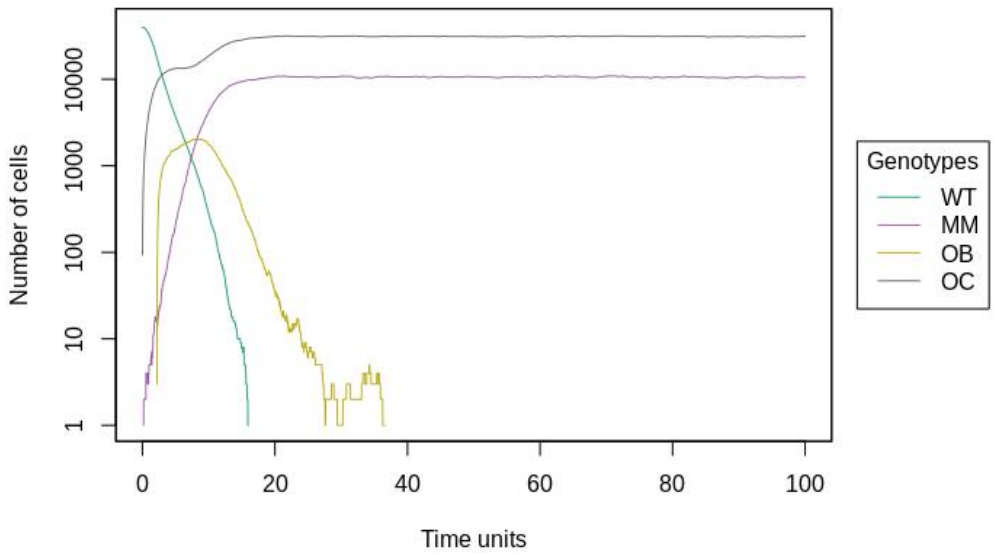


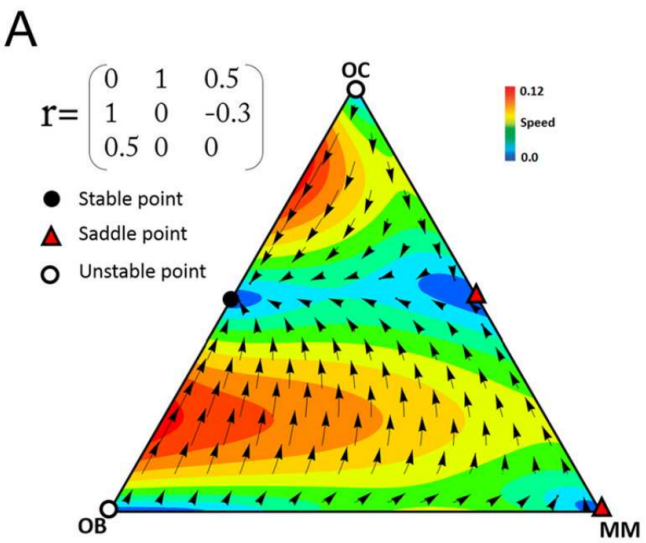
Fig 2. Example of the dynamics for scenario 1. In the presence of a small number of MM cells, the stable point on the OB-OC border becomes a saddle point and clonal selection leads to a stable coexistence of OC and MM cells. ($N = 10$, $c_3 = 1.4$, $c_2 = 1.2$, $c_1 = 1$). The arrows show the direction of the dynamics, and the colors show its speed (the euclidean distance between the frequencies at time t and t+1).

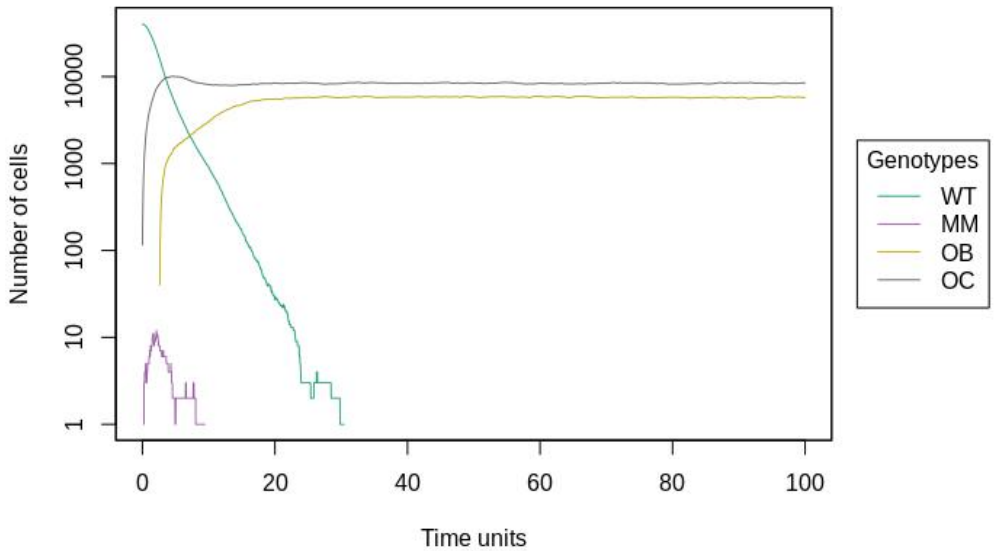
doi:10.1371/journal.pone.0168856.g002



Tumour-Stroma Interactions: Scenario 2

- $c_1 = c_2 = c_3$.
- The game has one polymorphic stable point between OB and OC. In this case, clonal selection leads to the regular OC-OB balance and prevents invasion of MM cells.





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