# Exercise 2: Frequency dependent fitness

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# Introduction

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# Additional functions: graphical summary

- **Box-plot:** graphical summary of the distribution of simulations results

**compositionPop2()**

```
## Extract and create a data frame with results from several simulations
compositionPop2 <- function(objPop, ...) {
  ## Create genotype names
  clon_labels <- c("WT", objPop[[1]]$geneNames)

  ## Extract the information to create a data frame
  listPop <- vapply(objPop, function(x) tail(x[[1]], 1)[1, -1],
                    as.double(1:length(clon_labels)))

  dfPop <- data.frame("Genotype" = rep(clon_labels,
                                       length(listPop)/length(clon_labels)),
                      "N" = c(listPop))
  simul_boxplot2(dfPop, ...)
}
```

Figure: Code for compositionPop2() function

# Additional functions: graphical summary

**simul_boxplot2()**

```r
## Plot box plot (by default same colors as plot.oncosimul type stream)
simul_boxplot2 <- function(df, main = FALSE, xlab = "Genotype", ylab = "N",
                           colors) {
  ## Create box plot, title and axis parameters
  e <- ggplot(df, aes(x = Genotype, y = N)) +
    theme(plot.title = element_text(hjust = 0.5, size = 16, face = "bold"),
          axis.title.x = element_text(size = 12, face = "bold"),
          axis.title.y = element_text(size = 12, face = "bold"),
          axis.text.x = element_text(size = 11),
          axis.text.y = element_text(size = 11))

  ## No title
  if (main == FALSE) {
    e + geom_boxplot(aes(fill = Genotype)) +
      stat_summary(fun.y = mean, geom = "point",
                   shape = 18, size = 2.5, color = "#FC4E07") +
      xlab(xlab) + ylab(ylab) +
      scale_fill_manual(values = colors)
      stat_summary(fun.y = mean, geom = "point",
                   shape = 18, size = 2.5, color = "#FC4E07") +
      xlab(xlab) + ylab(ylab) + scale_fill_manual(values = colors)}
  ## Title
  else {
    e + geom_boxplot(aes(fill = Genotype)) +
      stat_summary(fun.y = mean, geom = "point",
                   shape = 18, size = 2.5, color = "#FC4E07") +
      labs(title = main) +
      xlab(xlab) + ylab(ylab) + scale_fill_manual(values = colors)}
}
```

Figure: Code for simul_boxplot2() function

# Additional functions: graphical summary

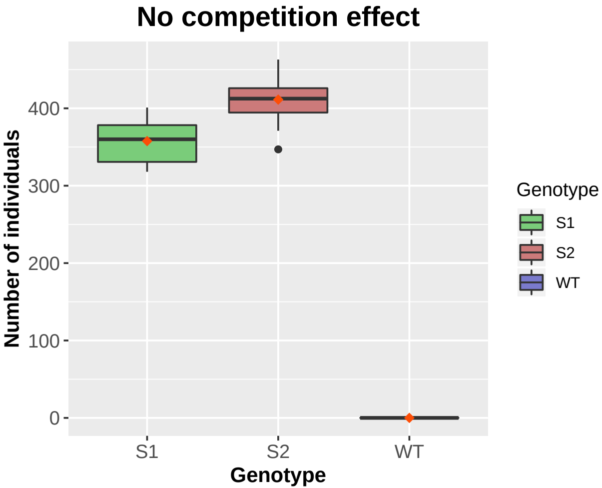
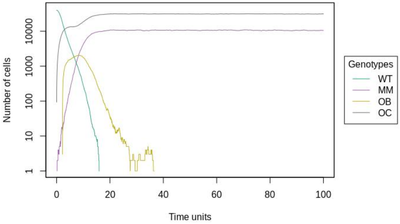
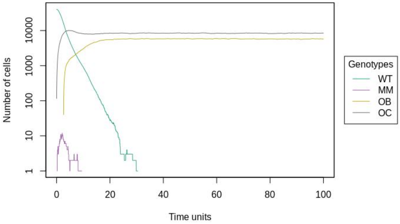



Figure: Box-plot from one of the Lotka-Volterra's example. 20 simulations were made

# Modification of the code

- **Legend**



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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.

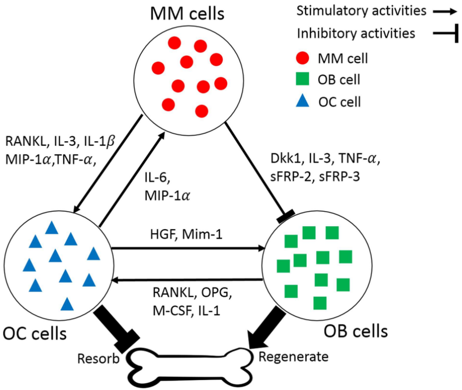


**Fig 1. Bone remodeling in multiple myeloma.** Multiple myeloma cells (MM) produce growth factors that activate osteoclasts (OC), which increase bone resorption, or that inhibit osteoblast (OB) differentiation. OC and OB secrete growth factors that affect each other and MM cells.

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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.

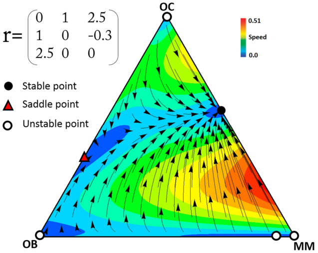
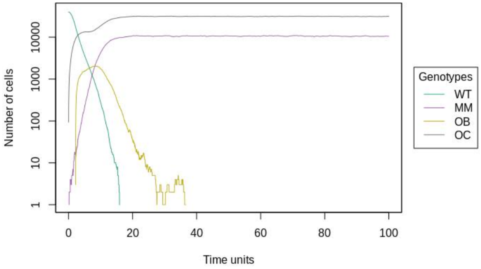


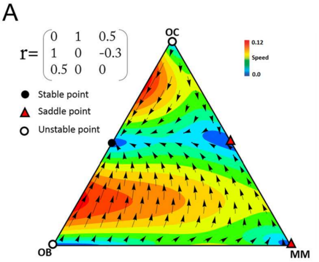

**Fig 2. Example of the dynamics for scenario 1.** In the presence of a small number of MM cells, the stable point on the OB-OC border becomes a saddle point and clonal selection leads to a stable coexistence of OC and MM cells. ($N = 10$, $c_3 = 1.4$, $c_2 = 1.2$, $c_1 = 1$). The arrows show the direction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

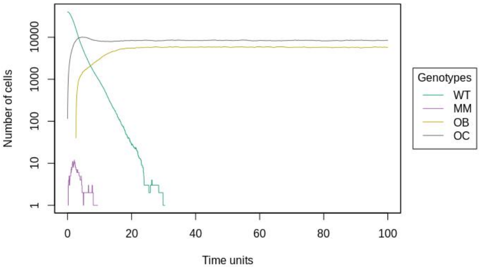
doi:10.1371/journal.pone.0168856.g002



# 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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