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Modeling the T-cells dynamics in lymphopenic conditions

We investigated division dynamics of two types of CD8 T-cells (OT1 and F5) in lymphopenic conditions. We used two markers: 1) CFSE (Carboxyfluorescein succinimidyl ester) – to calculate the number of divisions that the cells have made at a given time, 2) 7AAD (7-Aminoactinomycin D) – to determine in what period of cell cycle cells were at a given time.

A modified Smith-Martin model was used [1, 2] for the observed data. This model assume a cell cycle consisting of two parts: A-phase with stochastic duration and following after it B-phase with deterministic duration. There were four main parameters: transfer rate from A to B-phase λ, duration of B-phase Δ, time of triggering to division T_0 and death rate δ. To estimate them we used a minimization of the sum of weighted squared residuals with comparison of: 1) predicted and observed frequencies of cells with given number of divisions that was made to a given time, 2) predictions of fraction of cells in B-phase with observed fraction of 7AAD+ cells. Comparisons between models were performed using a cross-validation criterion.

It was found that OT1 cells divides faster (higher transfer rate λ and earlier triggering to division) than F5 cells. Duration of B-phase Δ was slightly higher for OT1 cells. Using the information from 7AAD marker together with CFSE data improved parameters identifiability.

References

[1] J. Smith, and L. Martin, *Do cells cycle?*, PNAS, **70**, 1263–1267, 1963.
[2] A. Yates, and M. Saini, A. Mathiot, B. Seddon, *Mathematical Modeling Reveals the Biological Program Regulating Lymphopenia-Induced Proliferation*, Journal of Immunology, **1800**, 1414–1422, 2008.