

Modeling Calcium Dynamics in T Cells

by Ida Hönigmann

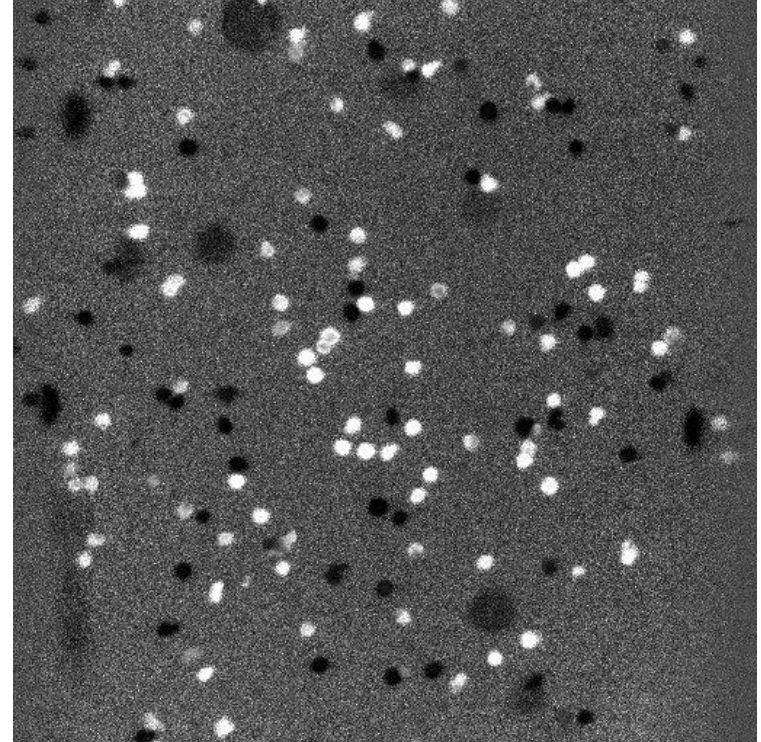
under supervision of Assistant Prof. Dr. Andreas Körner

Activation of T Cells

Necessary to be able to divide and perform immune response

Connection between t cell and antigen presenting cell

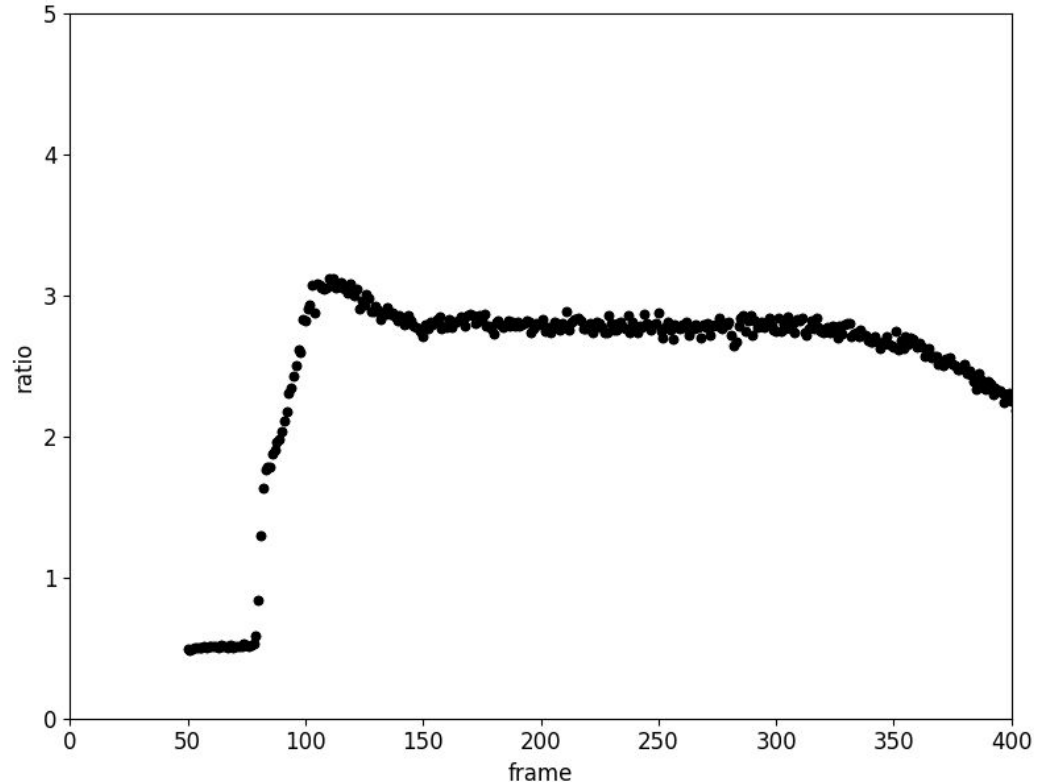
Correlation to calcium concentration



Calcium Concentration during Activation

Activation detected by hand or with subjective conditions

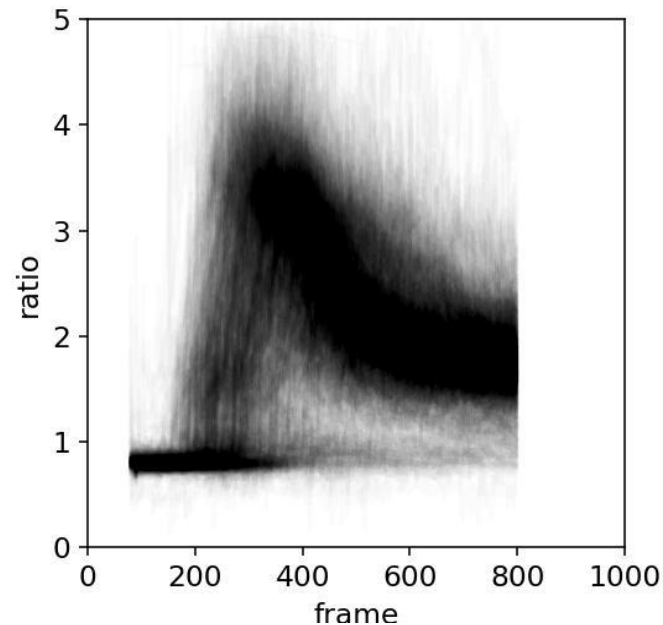
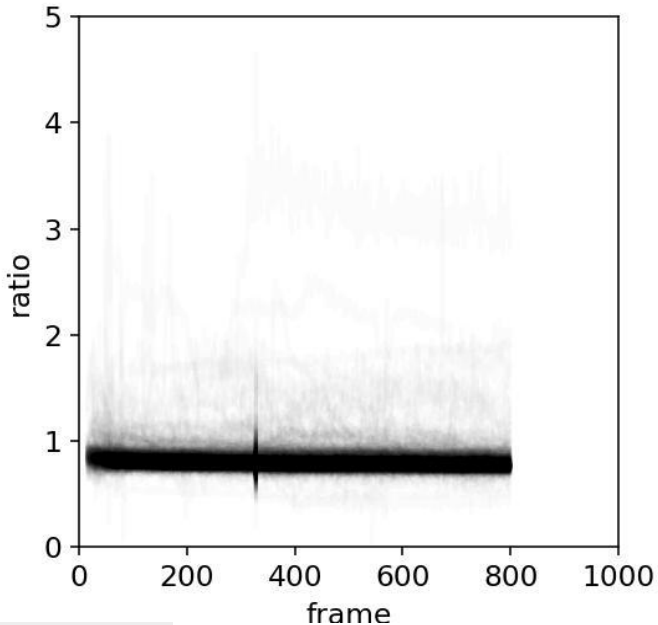
Objective: find algorithm which says whether t cell is activated without need for user input



Input Data

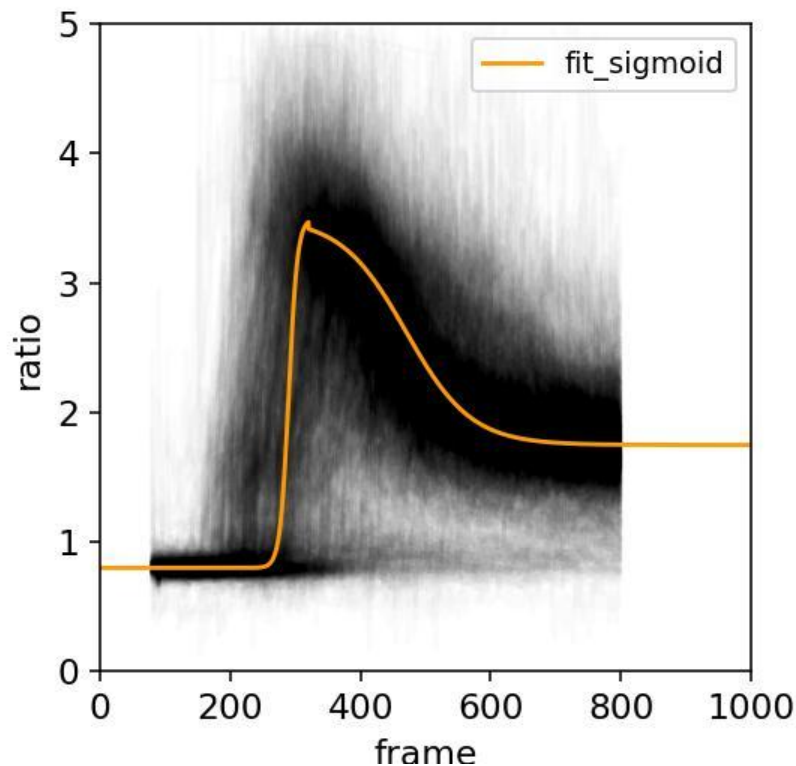
Positive and Negative Control of both mouse and human cells

Time series with about 700 values per t cell



Idea: Approximate Time Series with Simple Function

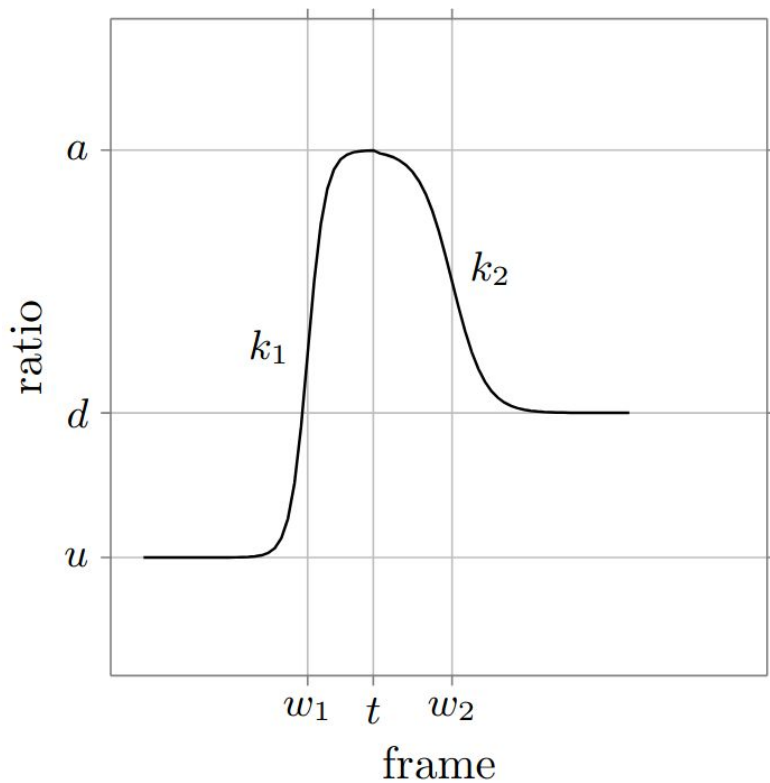
$$f_{ac}(x) := \begin{cases} \frac{a-u}{1+e^{-k_1(x-w_1)}} + u & \text{if } x \leq t \\ \frac{a-d}{1+e^{-k_2(x-w_2)}} + d & \text{else} \end{cases}$$



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Reduced 700 values into 7 values for each t cell!



Least Square Problem

Minimize $\sum_{k=1}^n |g_a(x_k) - y_k|^2$

Gauss-Newton

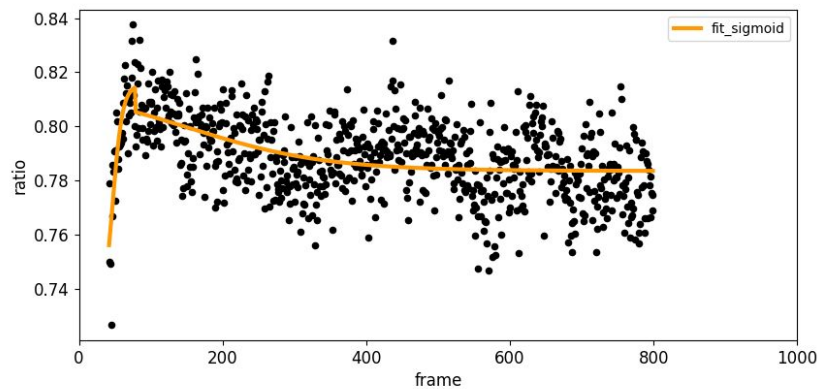
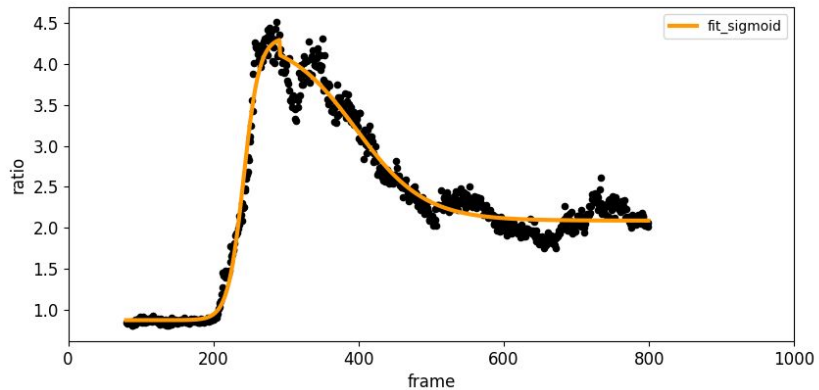
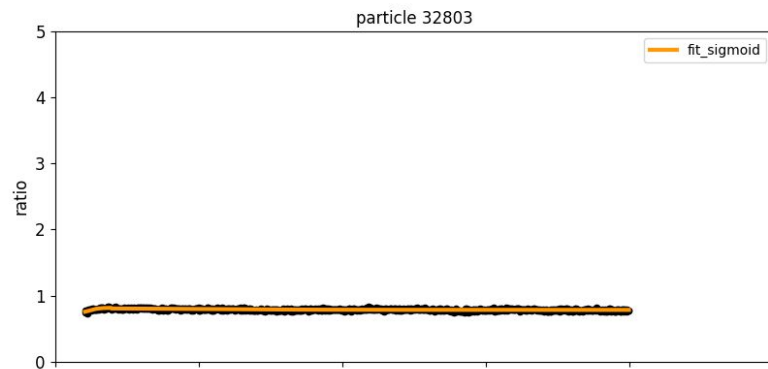
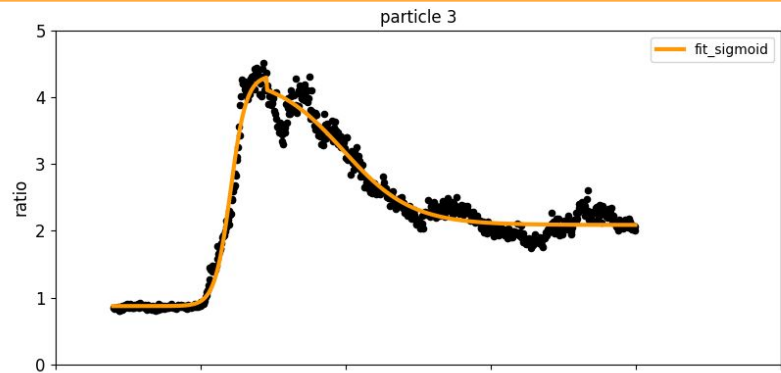
Levenberg-Marquardt

Bounded Problems

Trust Region Reflective

Dogleg Algorithm with Rectangular Trust Regions

Approximation



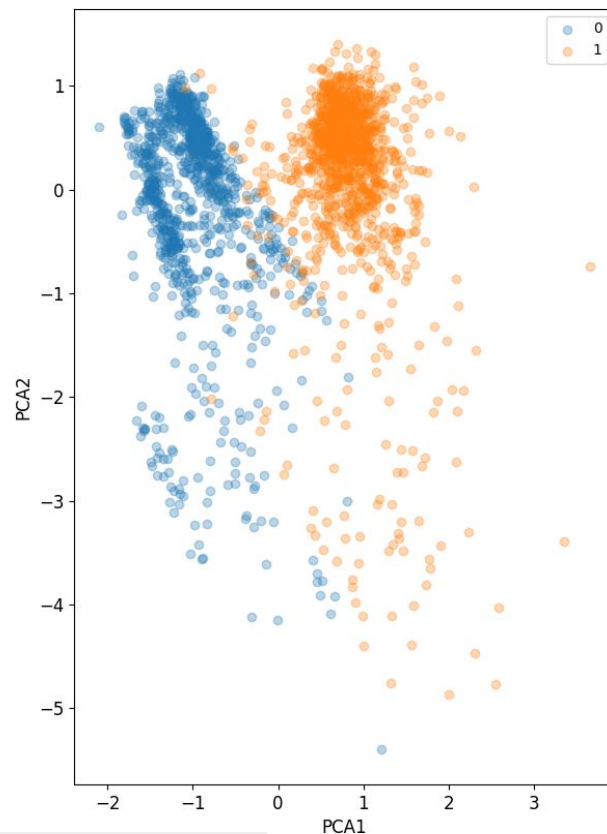
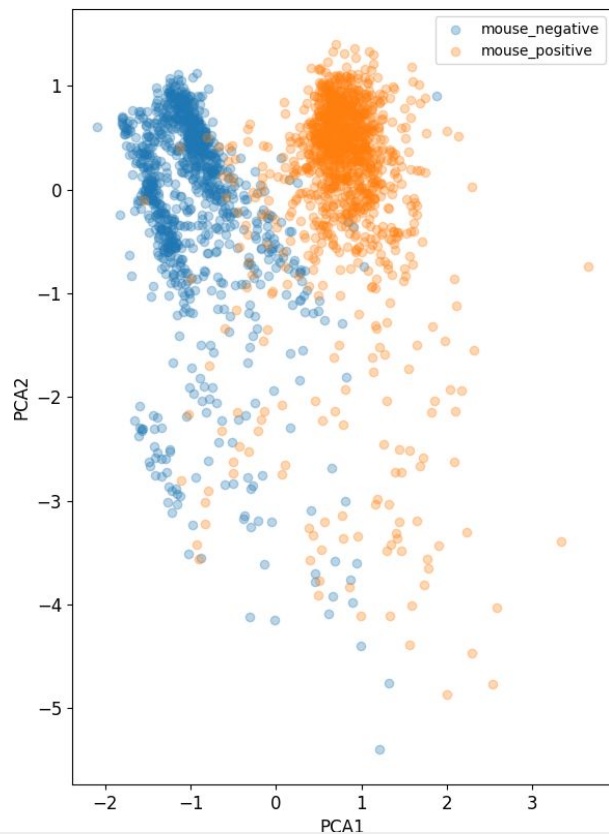
From Parameters to Measure of Activation

Clustering all 7 dimensional data points (hopefully) yields activation clusters

Gaussian Mixture Model gives means and std of normal distributions producing these clusters

KMeans gives means such that variances within a cluster are minimal

From Parameters to Measure of Activation



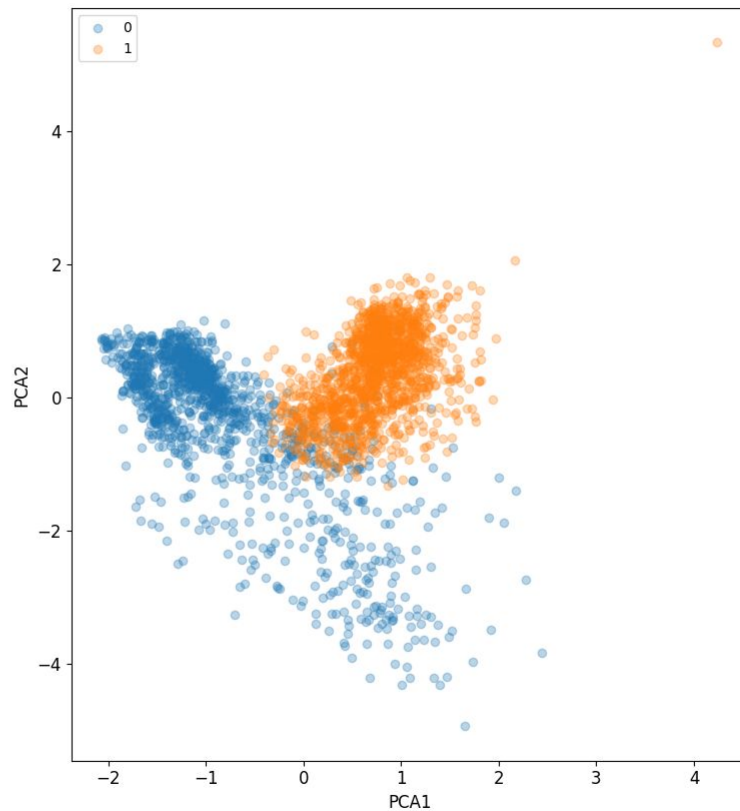
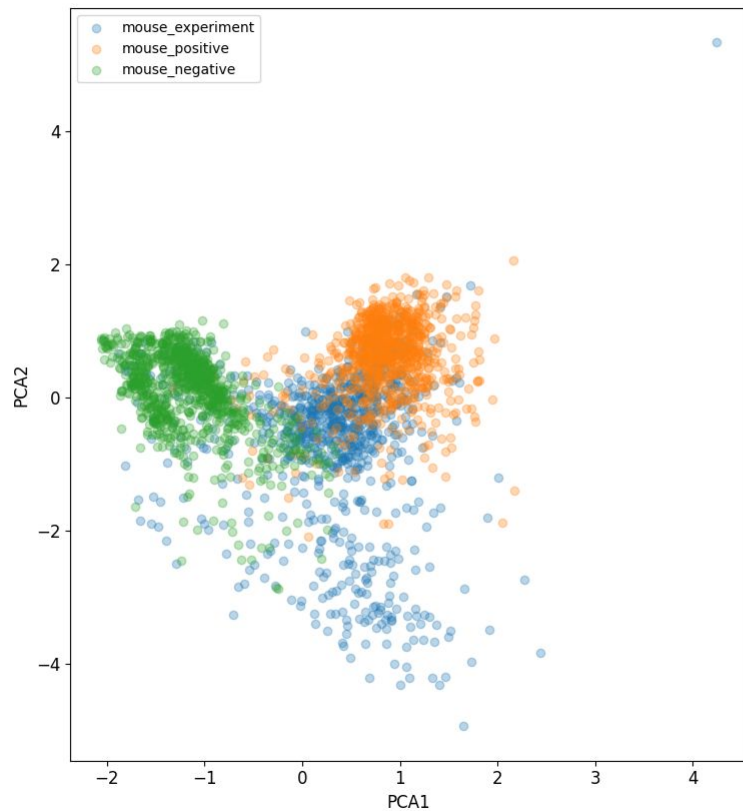
Proposed Algorithm

1. Get positive control, negative control and experiment recordings
2. Transform each t cell to parameters by using the approximation
4. Cluster parameters of negative and positive control into 2 clusters
5. Predict the membership of the experiment t cell parameters to the clusters to get a prediction of activation

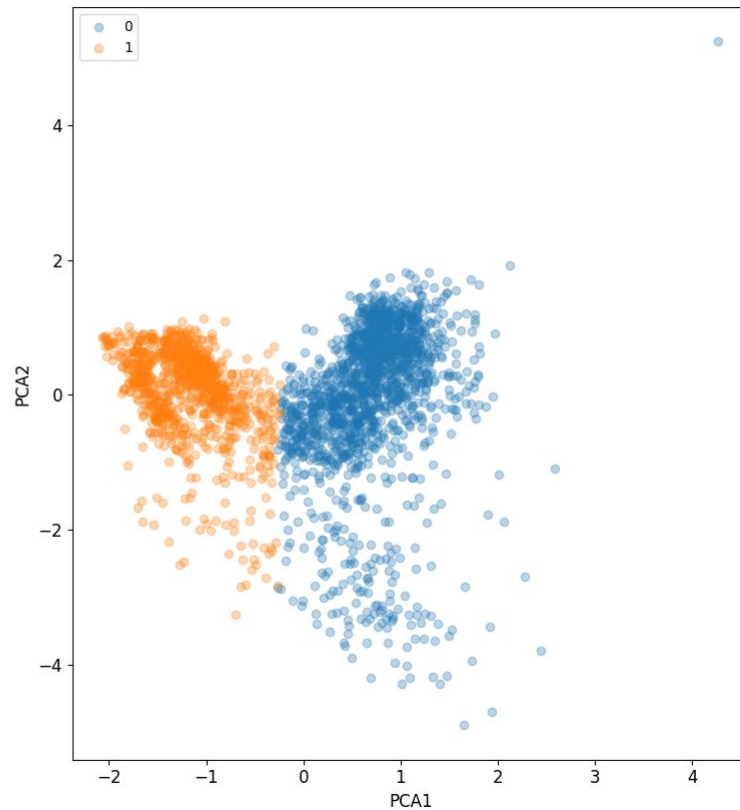
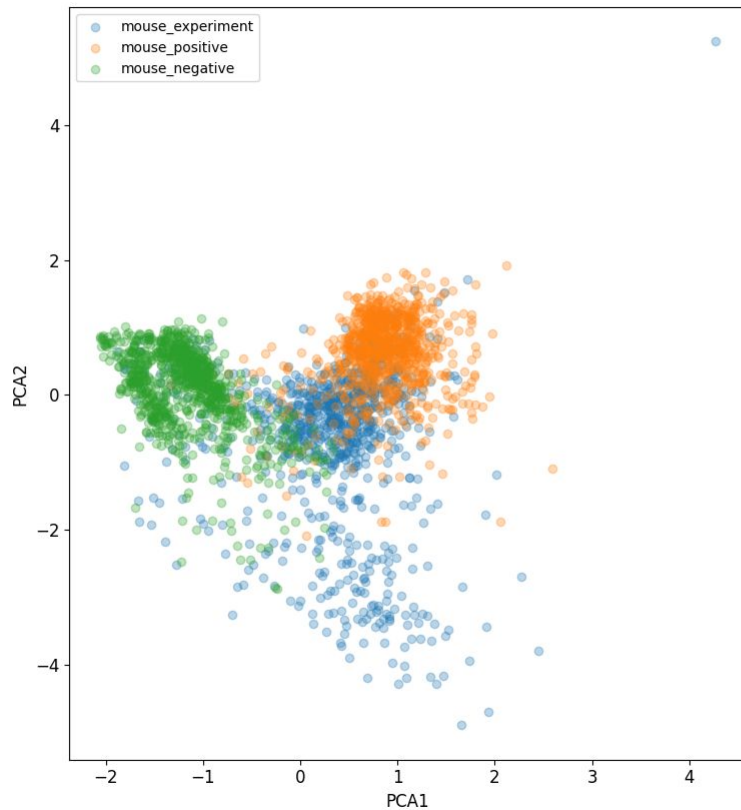
Proposed Algorithm

percentage activated	KMeans output	Gaussian Mixture output
0%	5.5%	4%
25%	27.5%	26%
50%	49.5%	49.5%
75%	72%	70.5%
100%	96%	97.5%

Proposed Algorithm

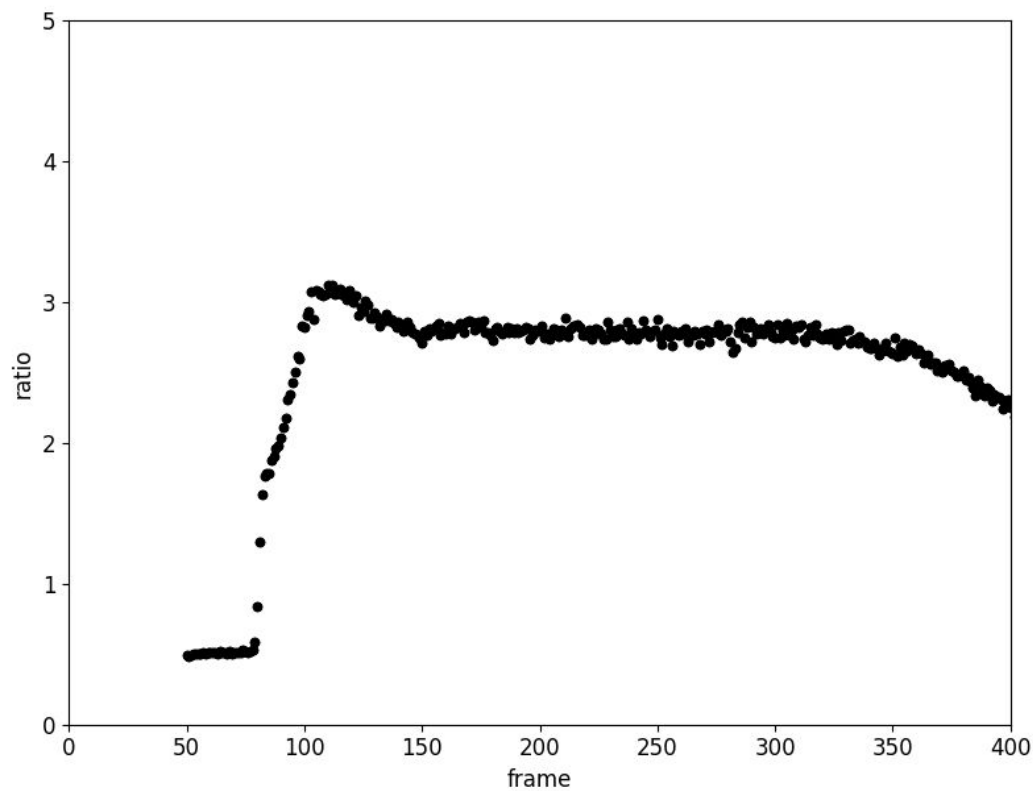


Proposed Algorithm

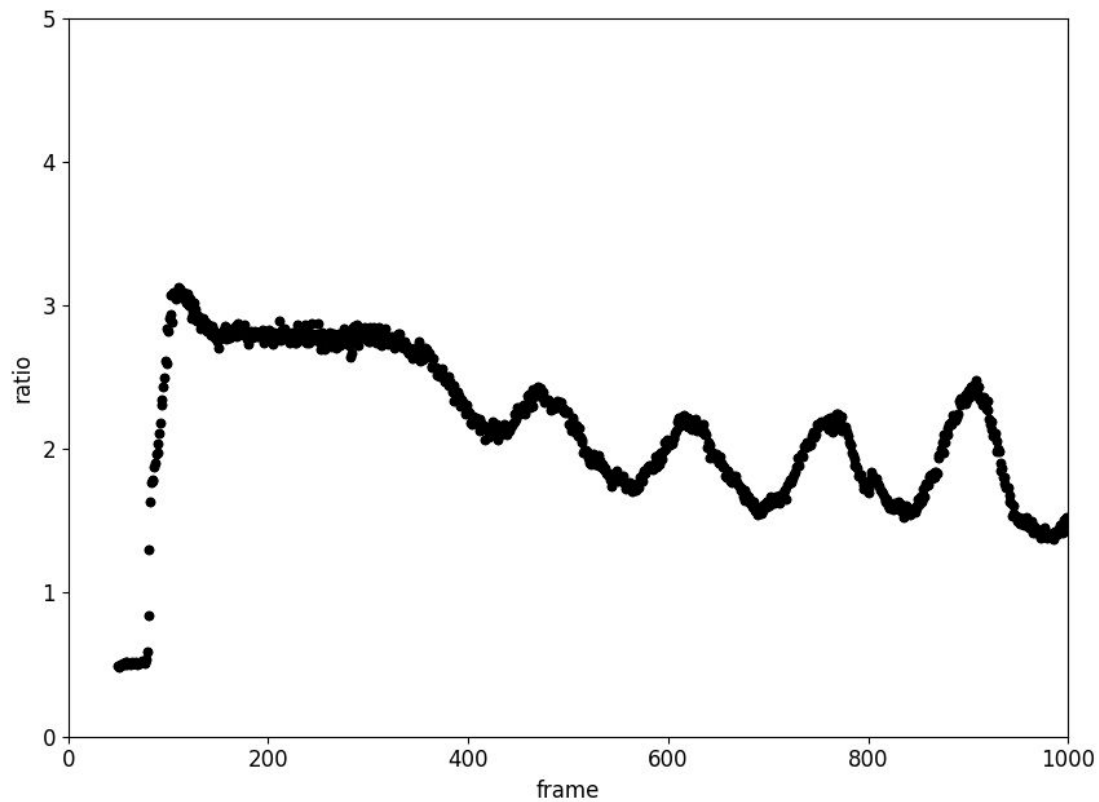


Questions

Oscillation



Oscillation



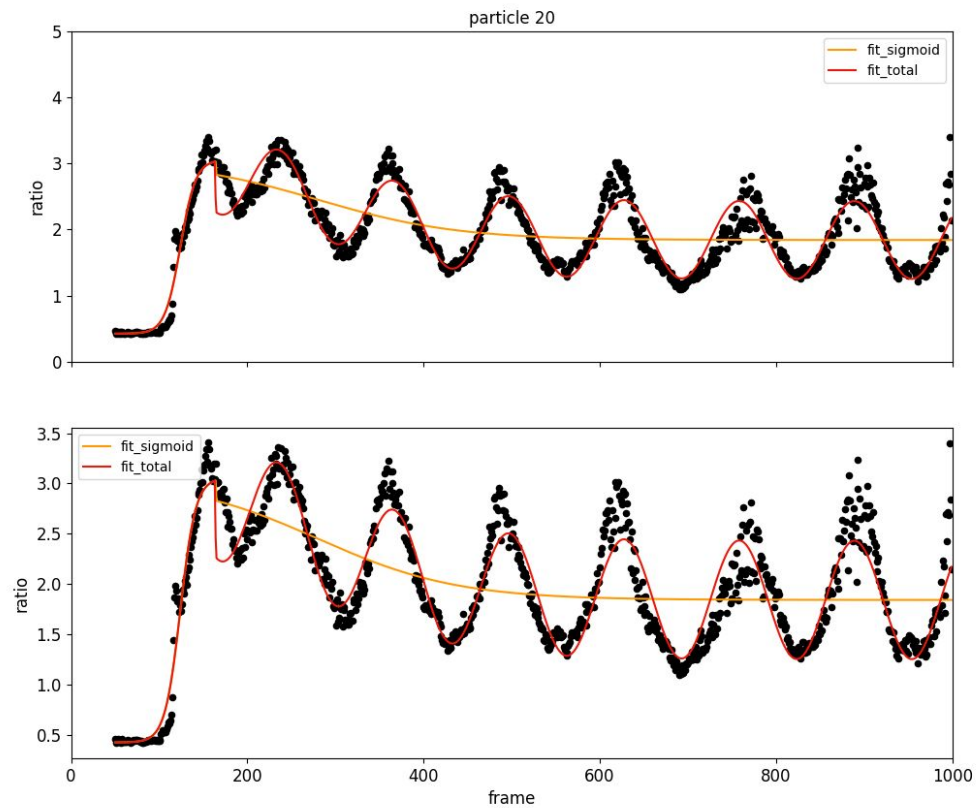
Oscillation

Fast Fourier Transformation to get initial guess for frequency

Approximate sin function as before

$$f(x, A, w, p) := A \cdot \sin(w \cdot t + p)$$

Oscillation



Components of T Cells

Relevant to changes in calcium concentration during activation

