

Modeling Calcium Dynamics in T Cells

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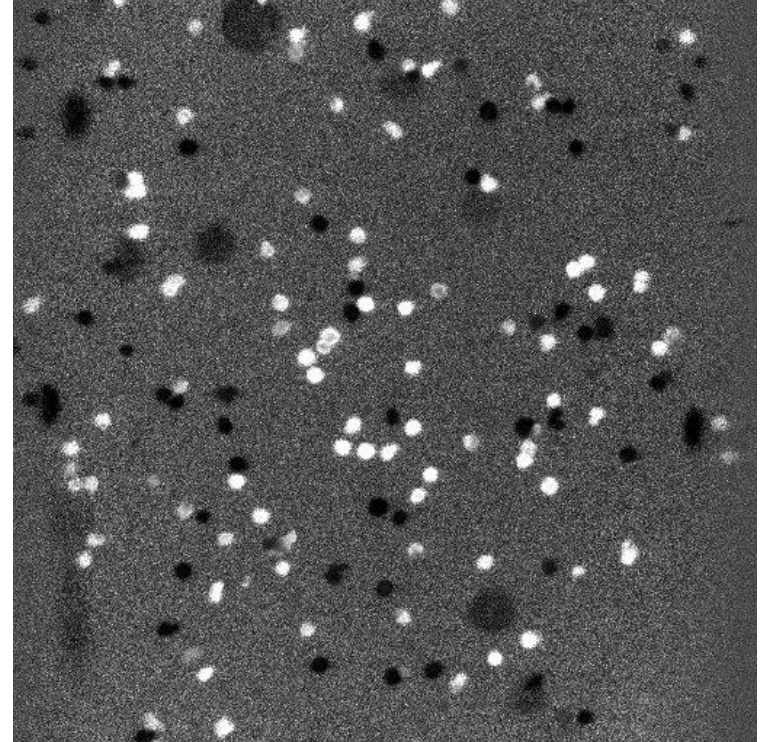
Activation of T Cells

Part of the immune response

Necessary to be able to divide and perform immune response

Connection between t cell and antigen presenting cell

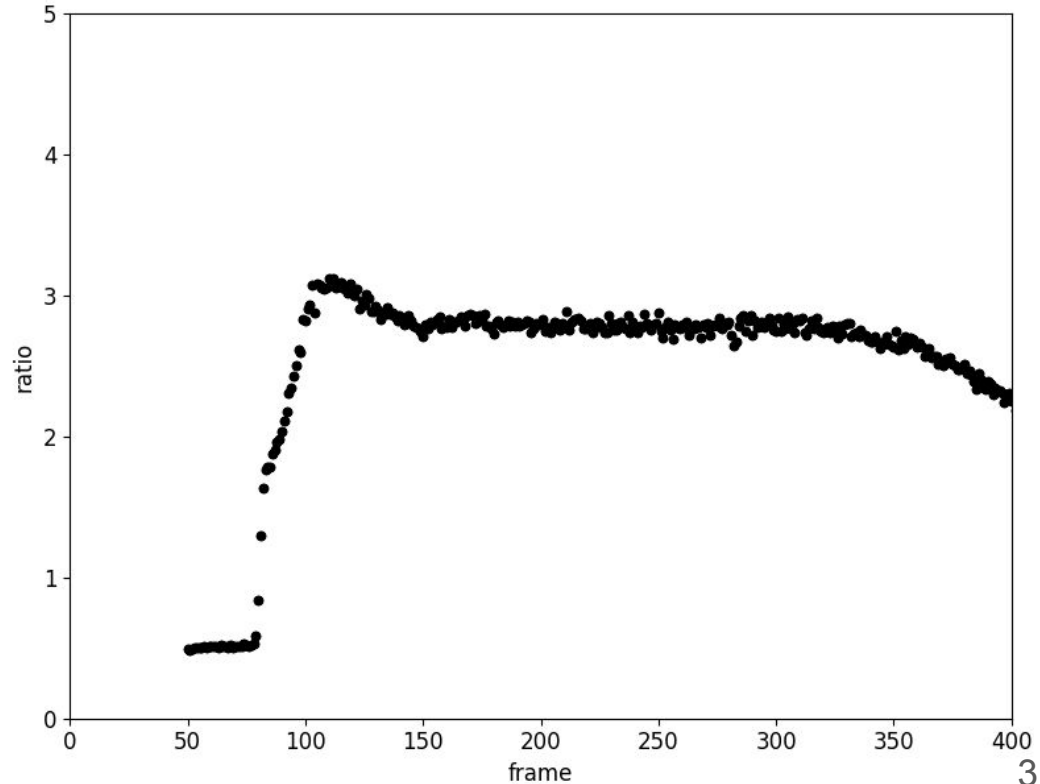
Correlation to calcium concentration



Calcium Concentration during Activation

Activation detected by hand or with subjective conditions

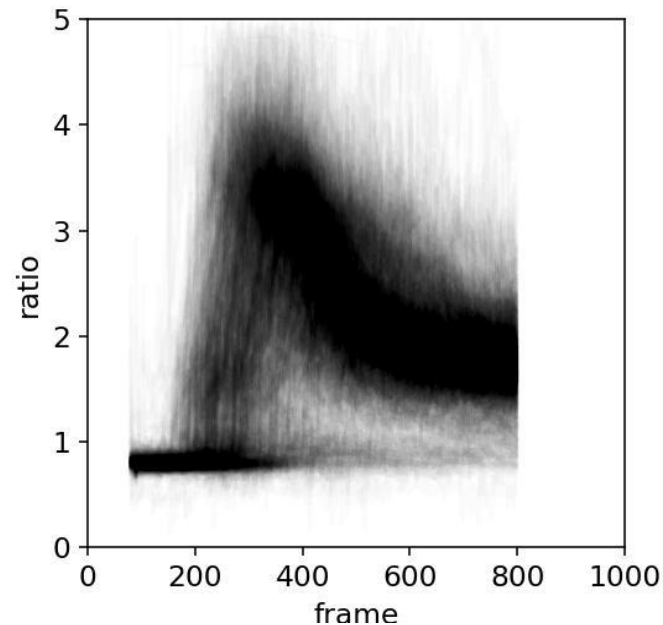
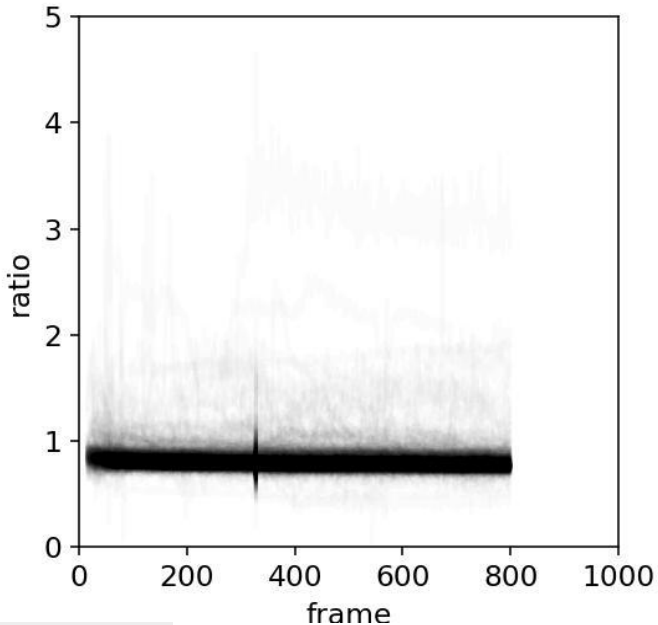
Objective: find algorithm which says whether t cell is activated without need for user input



Input Data

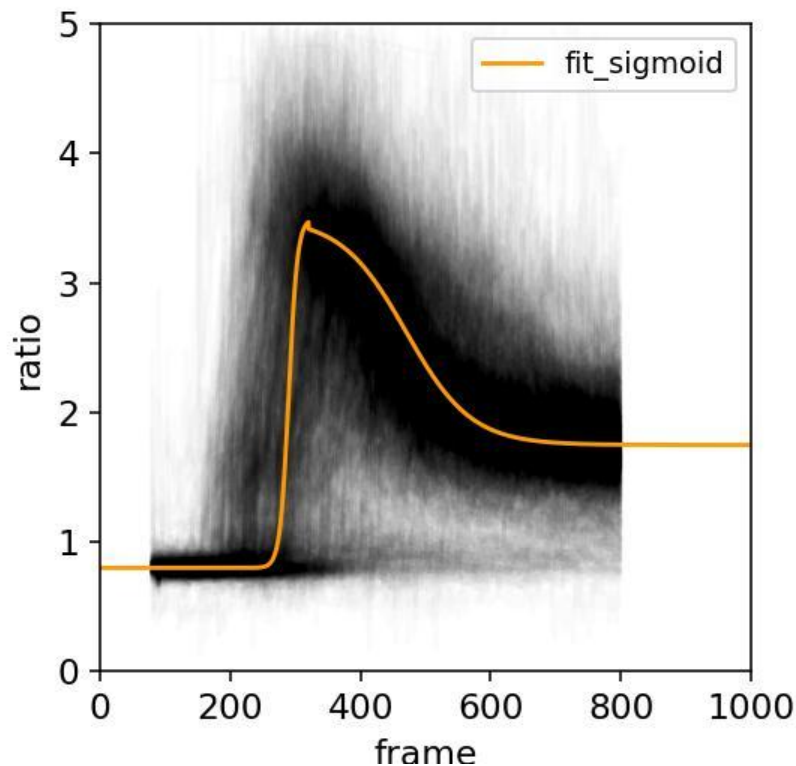
Positive and Negative Control of both mouse and human cells

Time series with about 700 values per t cell



Idea: Approximate Time Series with Simple Function

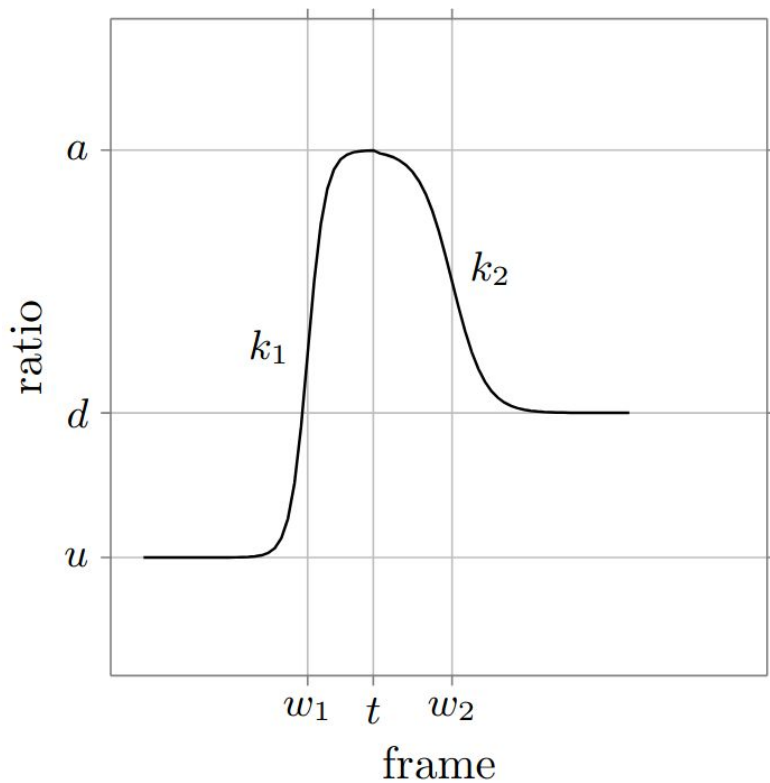
$$f_{ac}(x) := \begin{cases} \frac{a-u}{1+e^{-k_1(x-w_1)}} + u & \text{if } x \leq t \\ \frac{a-d}{1+e^{-k_2(x-w_2)}} + d & \text{else} \end{cases}$$



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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

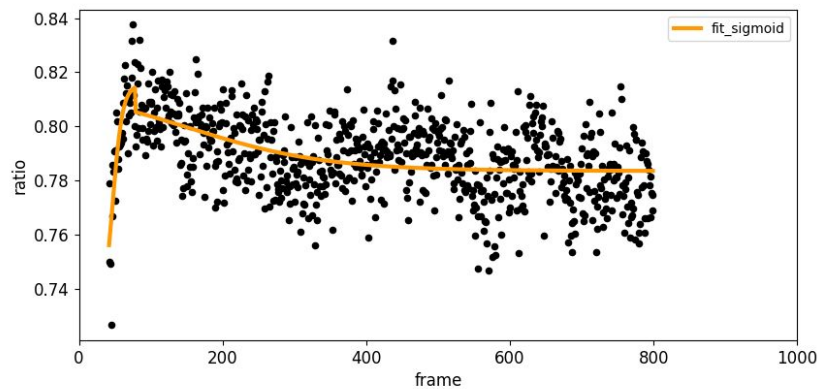
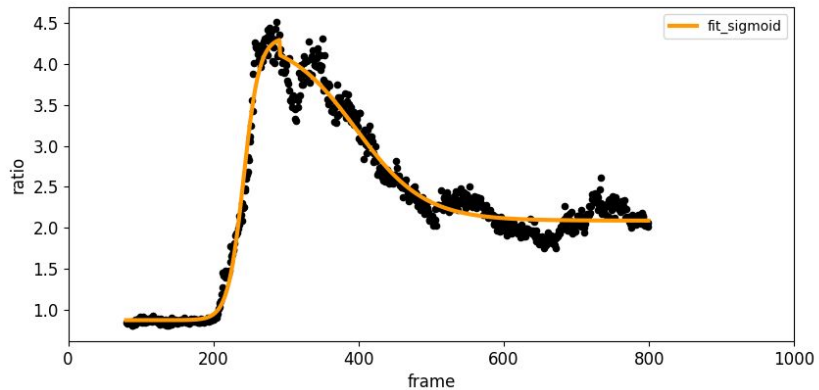
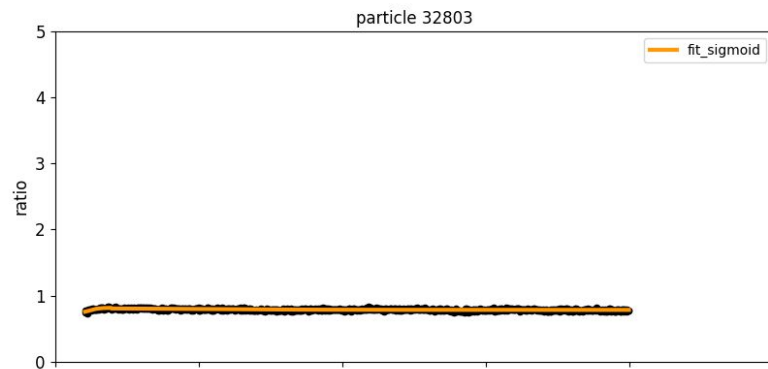
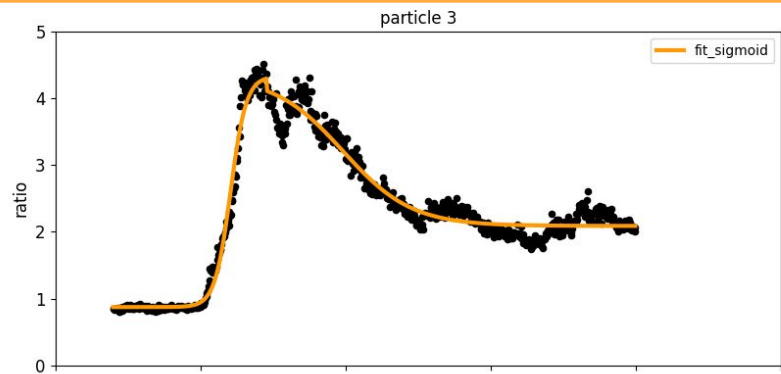
Levenberg-Marquardt

Bounded Problems

Trust Region Reflective

Dogleg Algorithm with Rectangular Trust Regions

Approximation



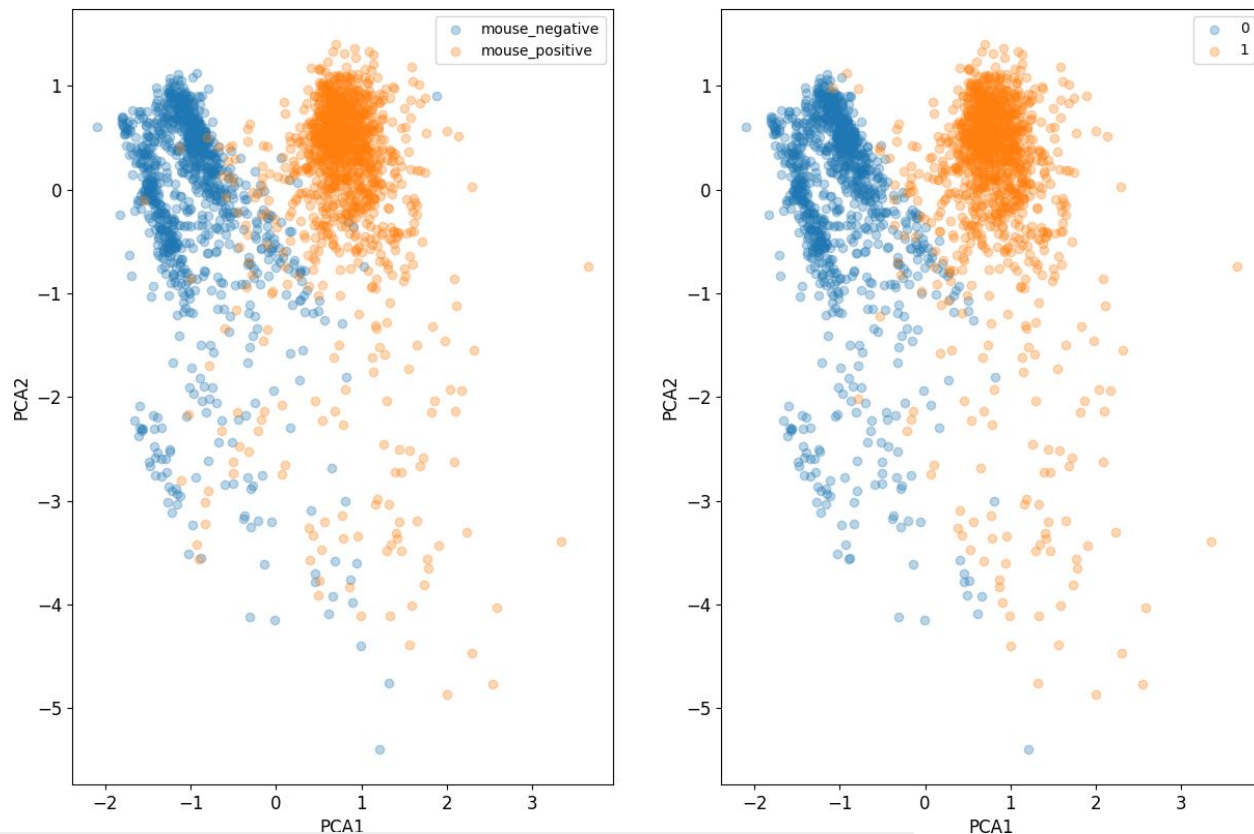
From Parameters to Measure of Activation

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



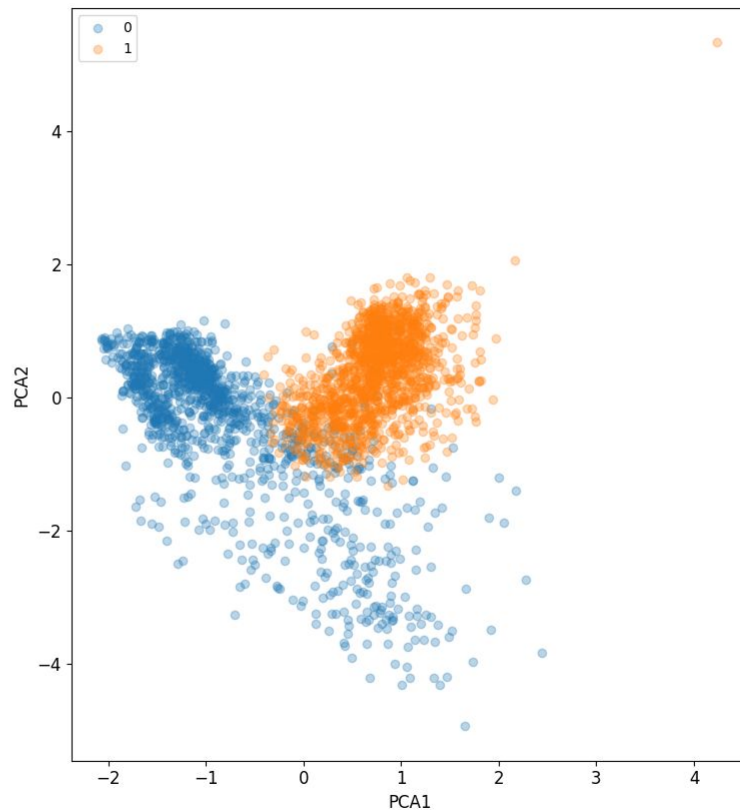
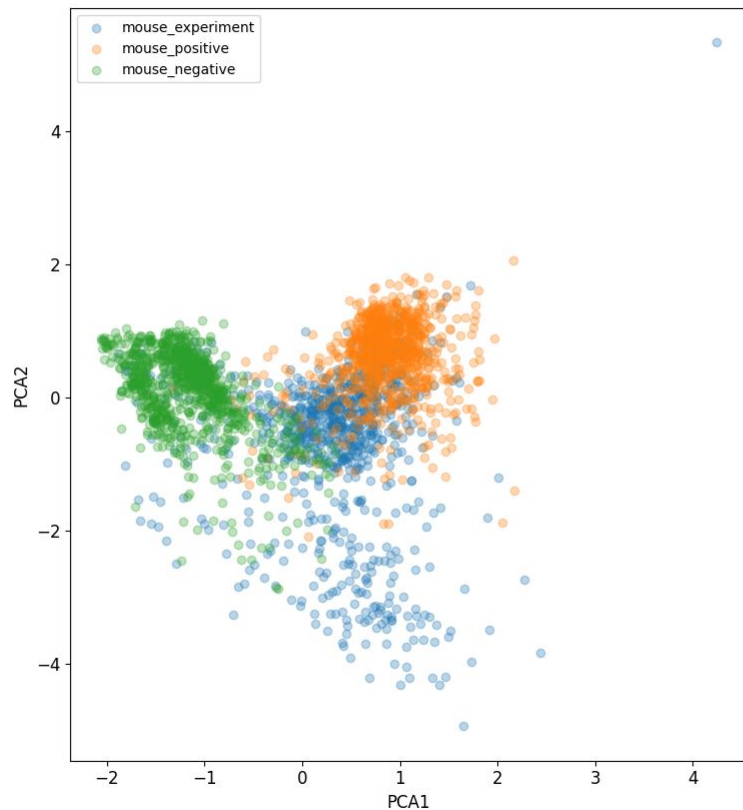
Proposed Algorithm

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

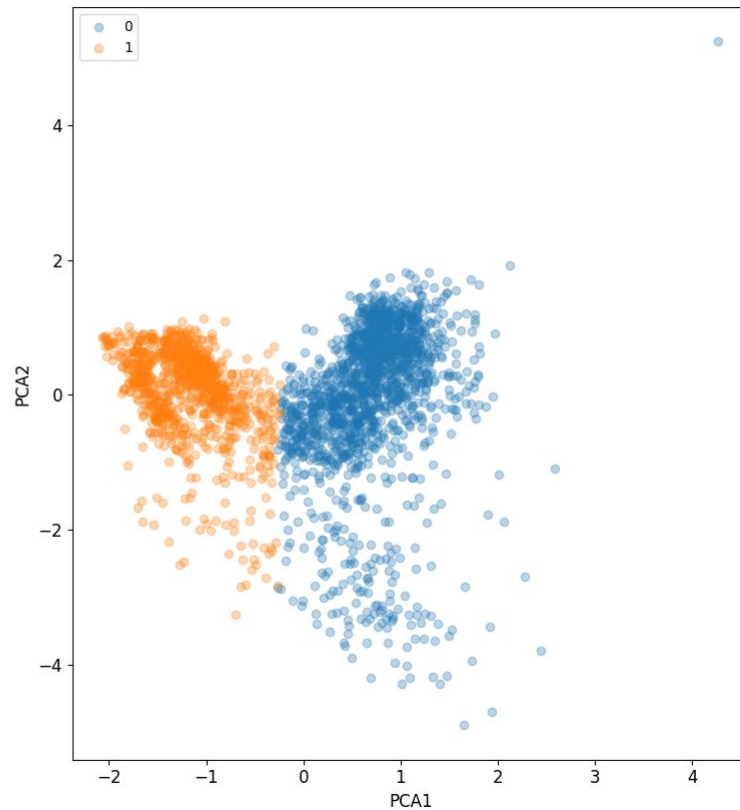
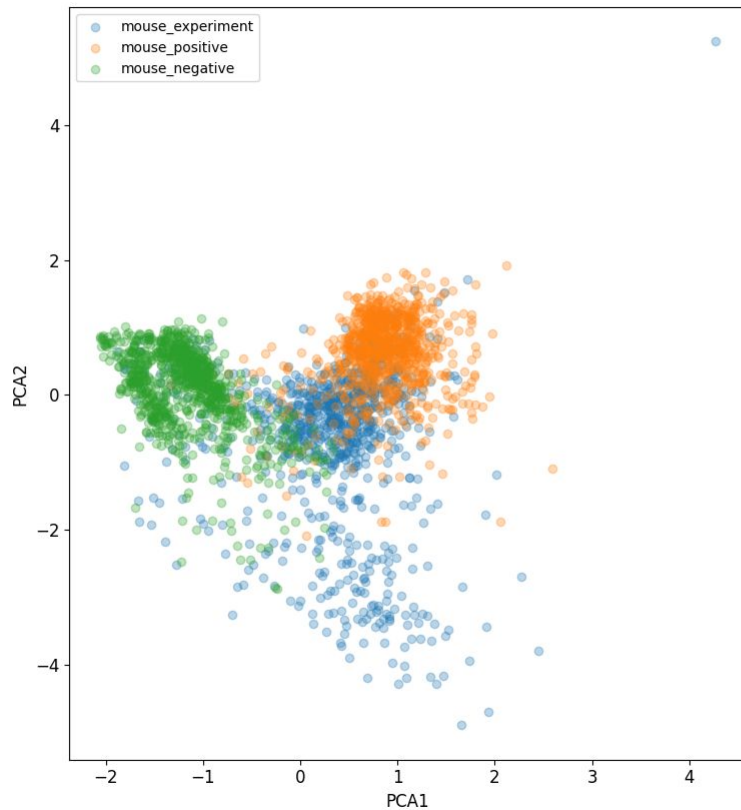
Classification Results

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%

Gaussian Mixture Model Applied



KMeans Applied



Discussion

Objective algorithm for counting number of activated t cells

Open questions:

- Accuracy?
- Differences between KMeans and Gaussian Mixture Model
- Types of activated t cells

Discussion

+ Questions

Objective algorithm for counting number of activated t cells

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Accuracy Measure - Cohen's Kappa

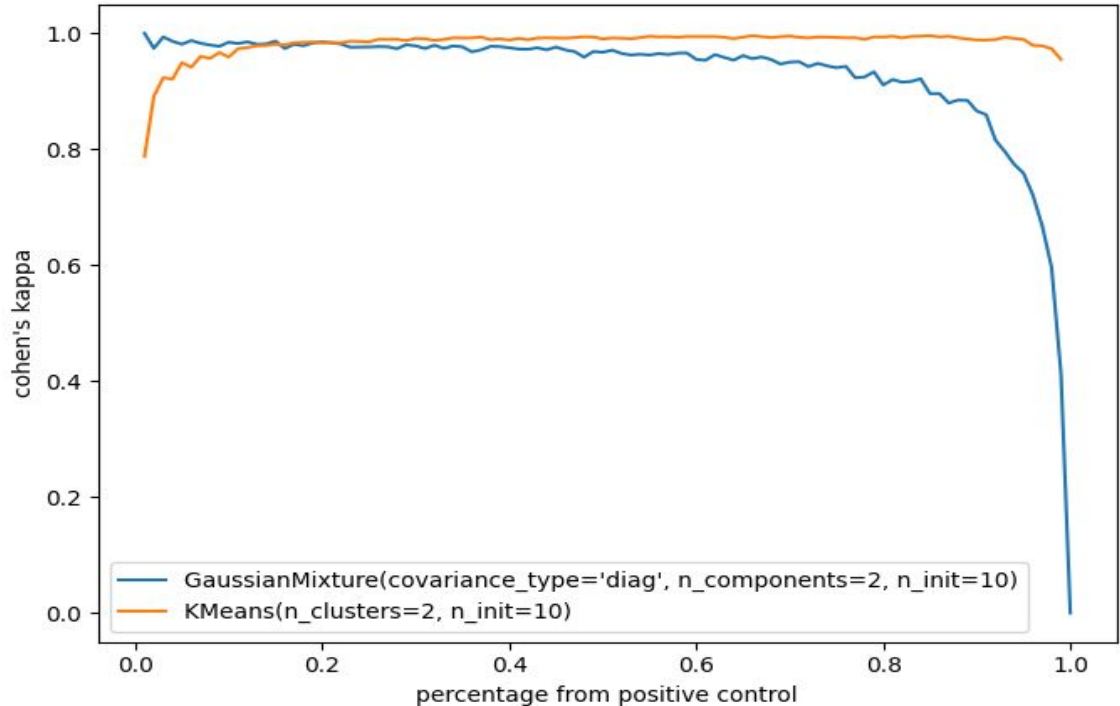
Confusion matrix to a single value via Cohen's Kappa

TP	FN
FP	TN

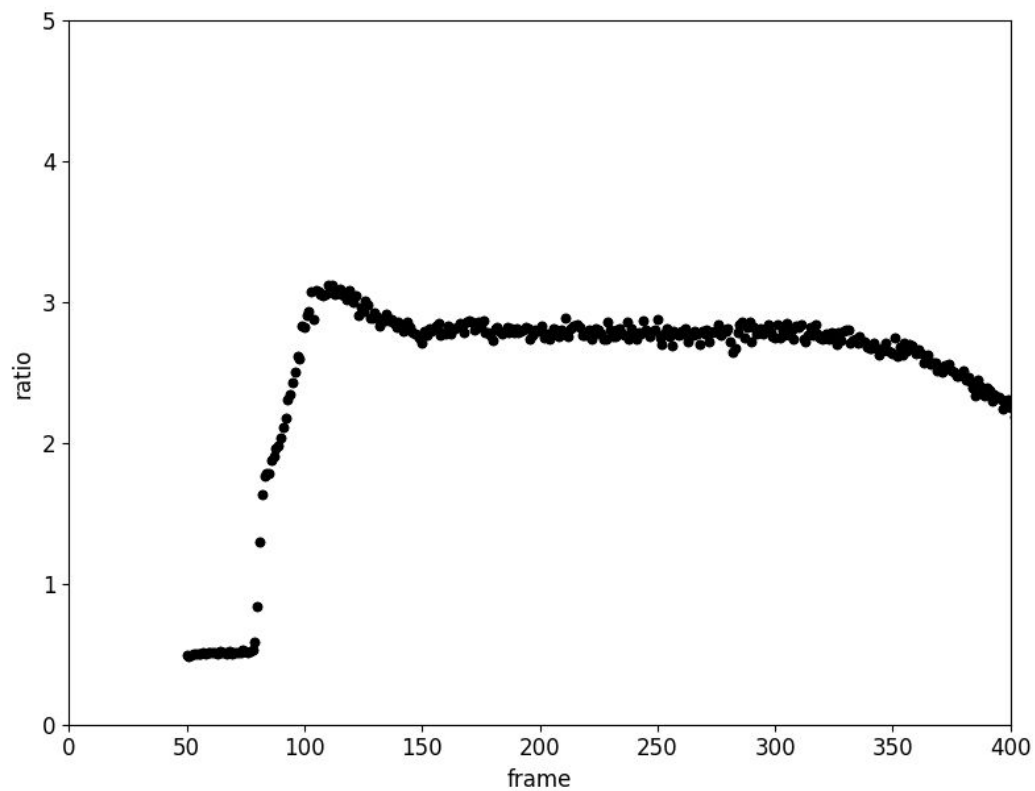
$$\kappa \equiv \frac{p_o - p_e}{1 - p_e} = 1 - \frac{1 - p_o}{1 - p_e}$$

p_o ... Observed agreement

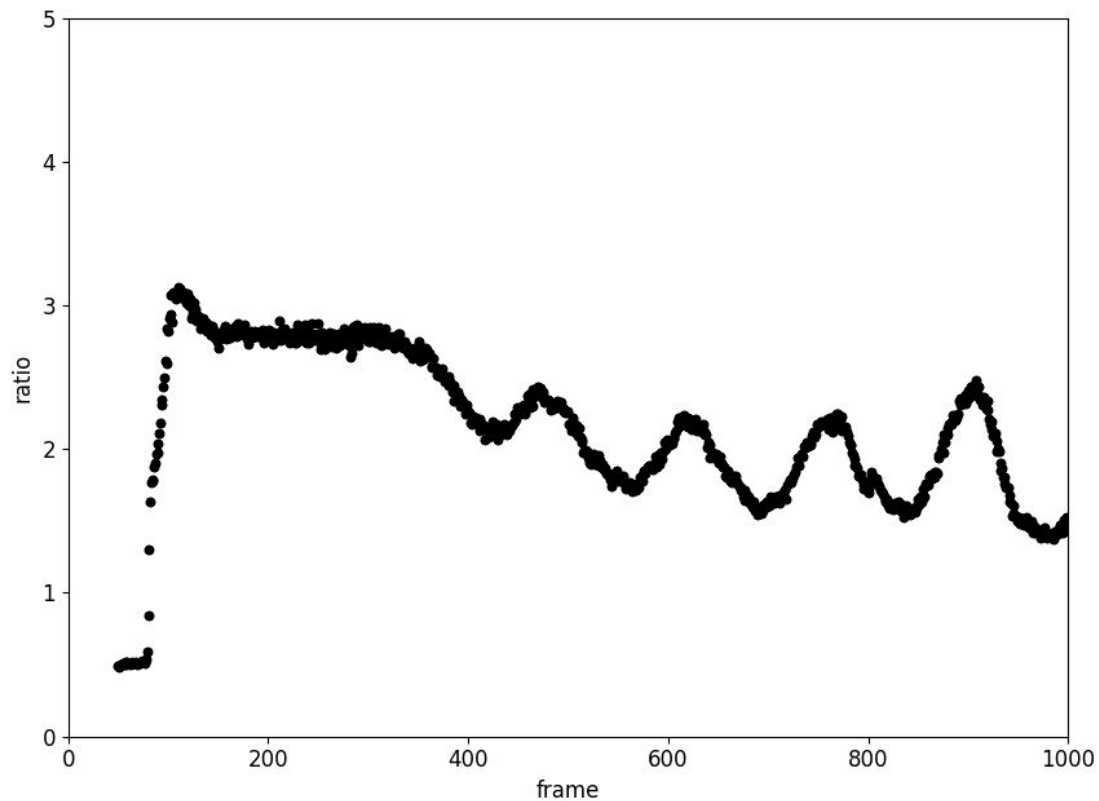
p_e ... Probability of agreement by chance



Oscillation



Oscillation



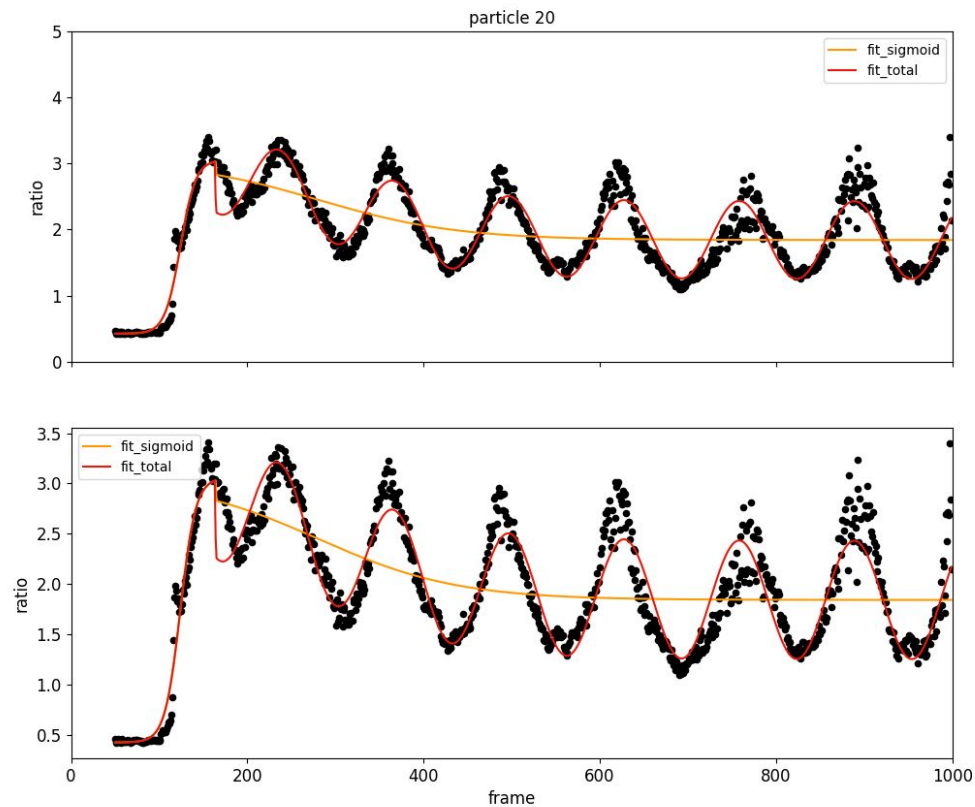
Oscillation

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

