A brief intro to Explainable AI and its application to antibody screening

28.03.2023

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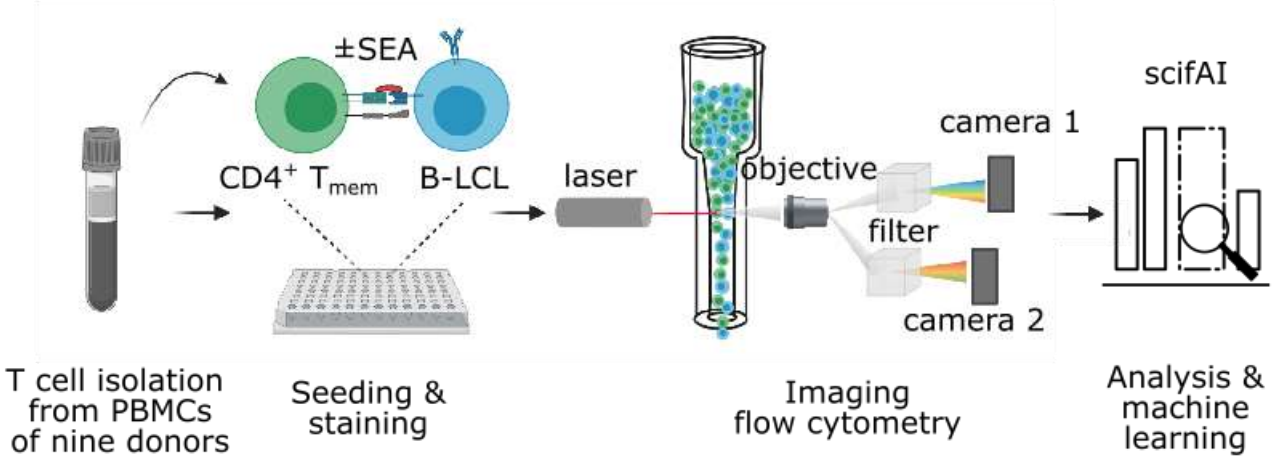
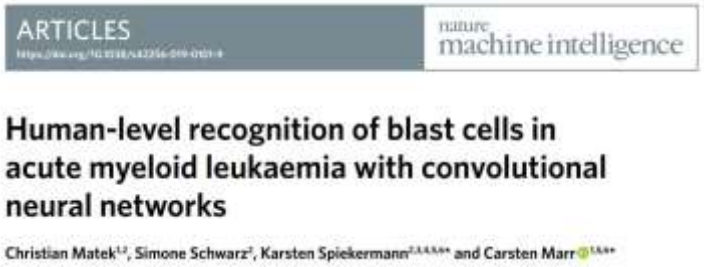
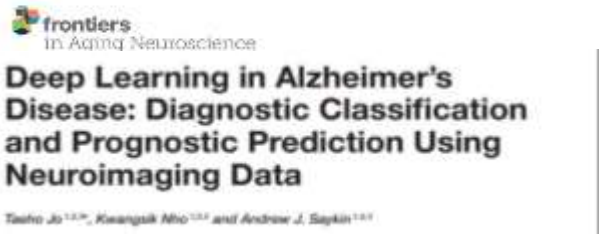


Part 1: intro to explainable AI

Motivation

- Recent advances in machine learning have been efficient for essential tasks in diagnostics and have reached the human level or even outperformed experts.





- However, the black-box nature of algorithms has restricted their clinical use.

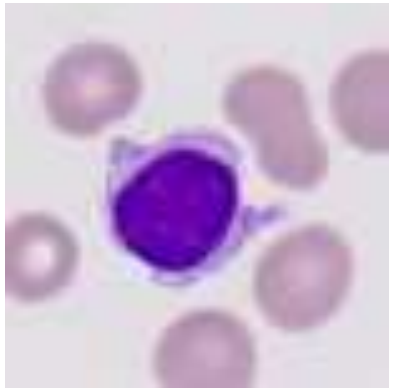
Practical example

Let‘s imagine that we have trained an algorithm that can distriminate between Mylocites and typical Lymphocytes:

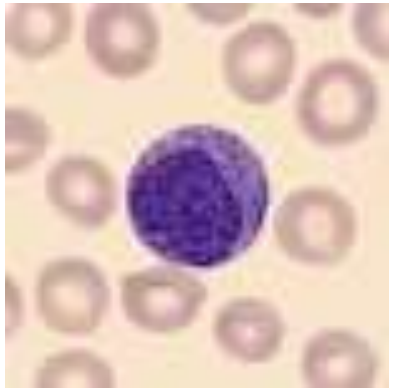
Q) Did the model use the background color?

Q) What is the exact difference that the model has noticed?

Explainability must be used to answer such questions!



Typical Lymphocytes



Myelocyte

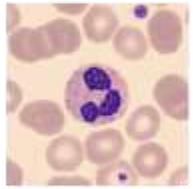
Matek, C., Schwarz, S., Spiekermann, K. et al. Human-level recognition of blast cells in acute myeloid leukaemia with convolutional neural networks. Nat Mach Intell 1, 538–544 (2019). https://doi.org/10.1038/s42256-019-0101-9

Acevedo A. et al. A dataset of microscopic peripheral blood cell images for development of automatic recognition systems. Data in Brief, Volume 30, (2020) https://doi.org/10.1016/j.dib.2020.105474

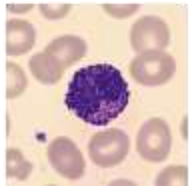
General classification pipeline

Lymphocyte typical

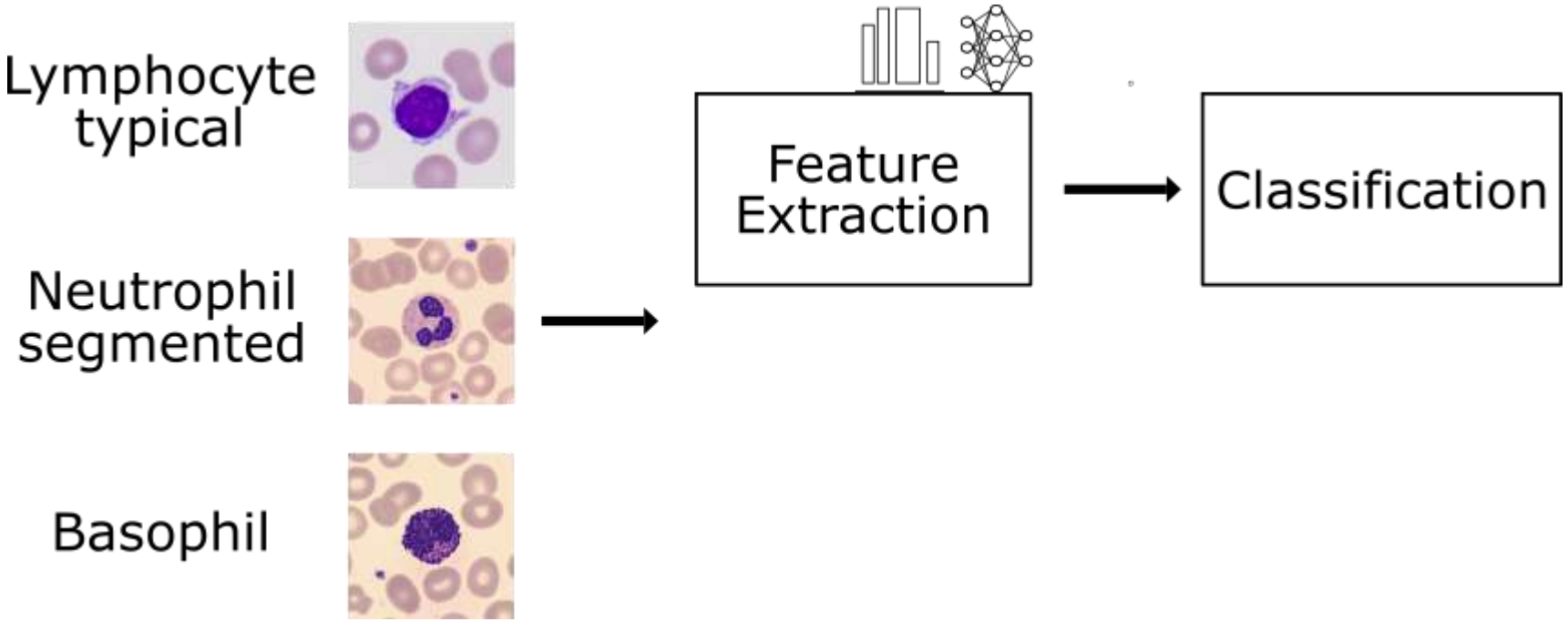
Neutrophil segmented



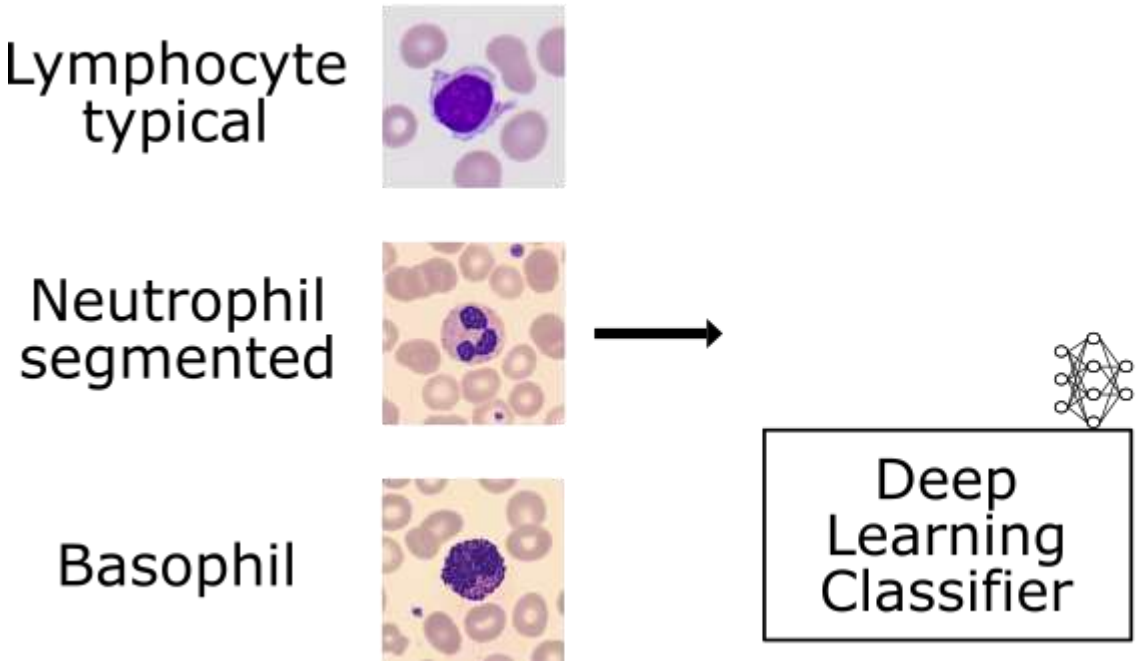
Basophil



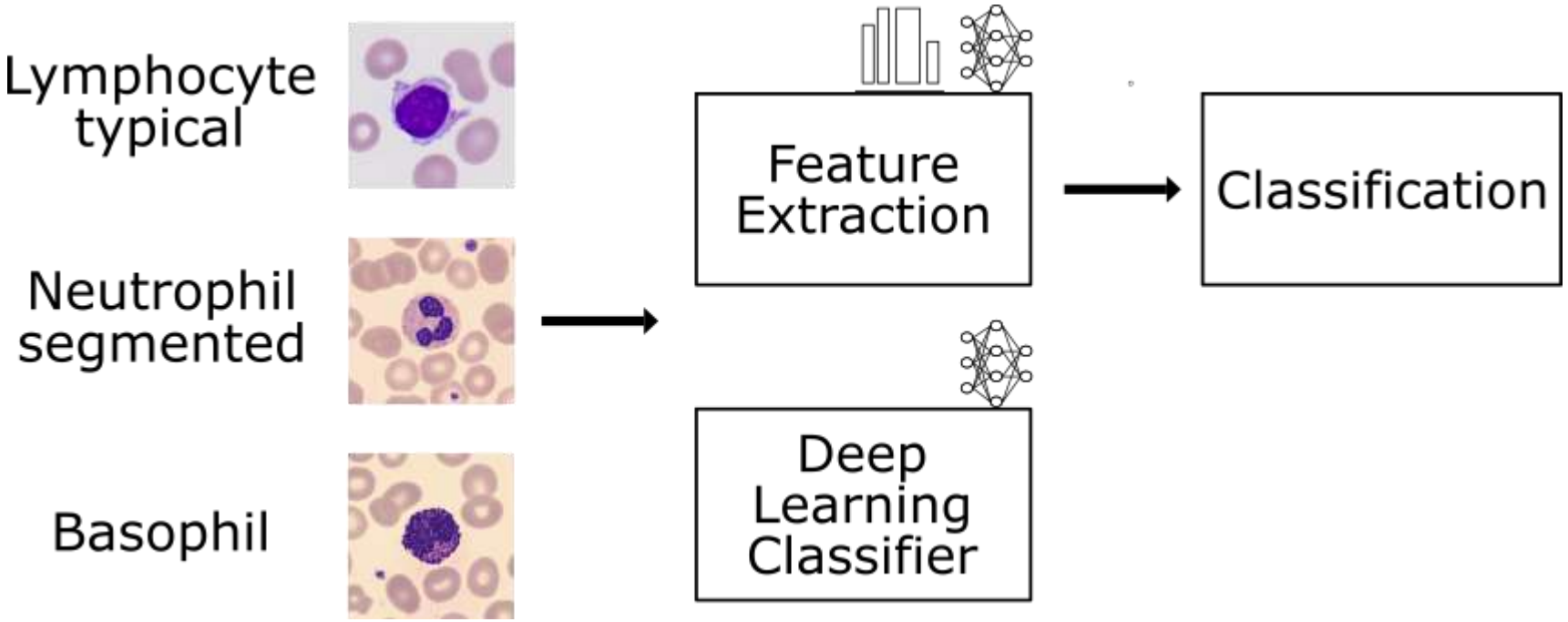
General classification pipeline



General classification pipeline

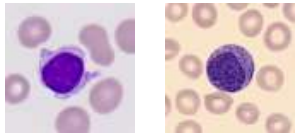


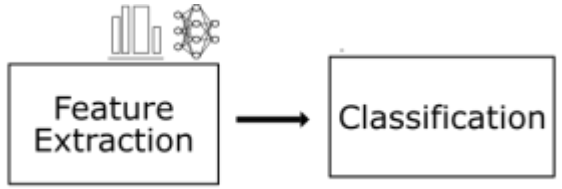
General classification pipeline



How can we explain each pipeline?

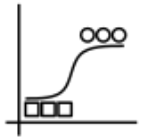
Explainability





In-model

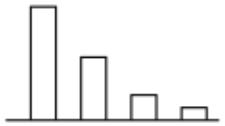
Random Forest



Linear Models

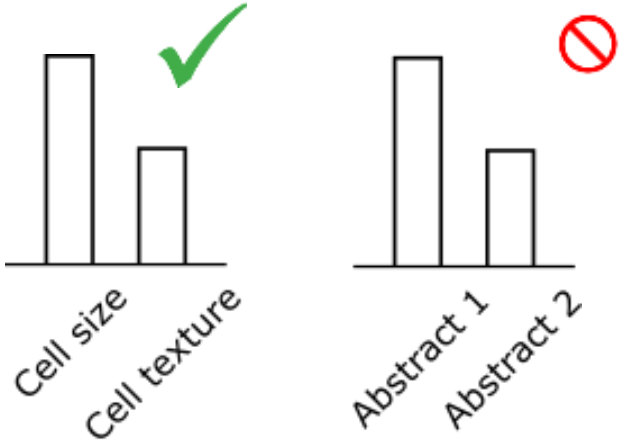
Post-model

SHAP values



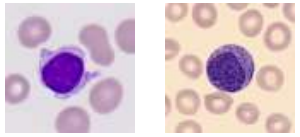
Permutation importance

- Needs meaningful features



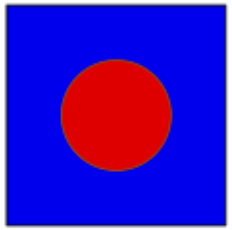
- Suffers from multi-dimensionality
- Suffers from multi-collinearity

Explainability

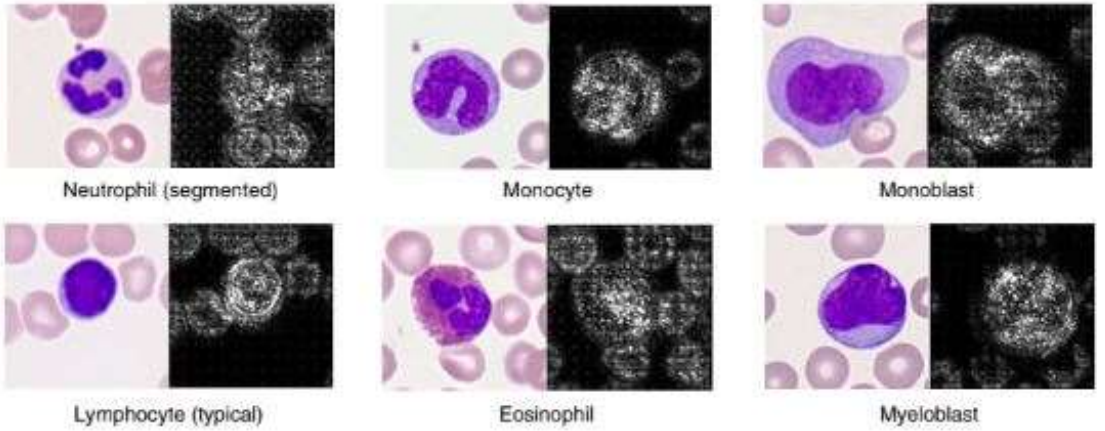


- Work as sanity checks
- Cannot provide meaningful insights

Post-model



Pixel importance



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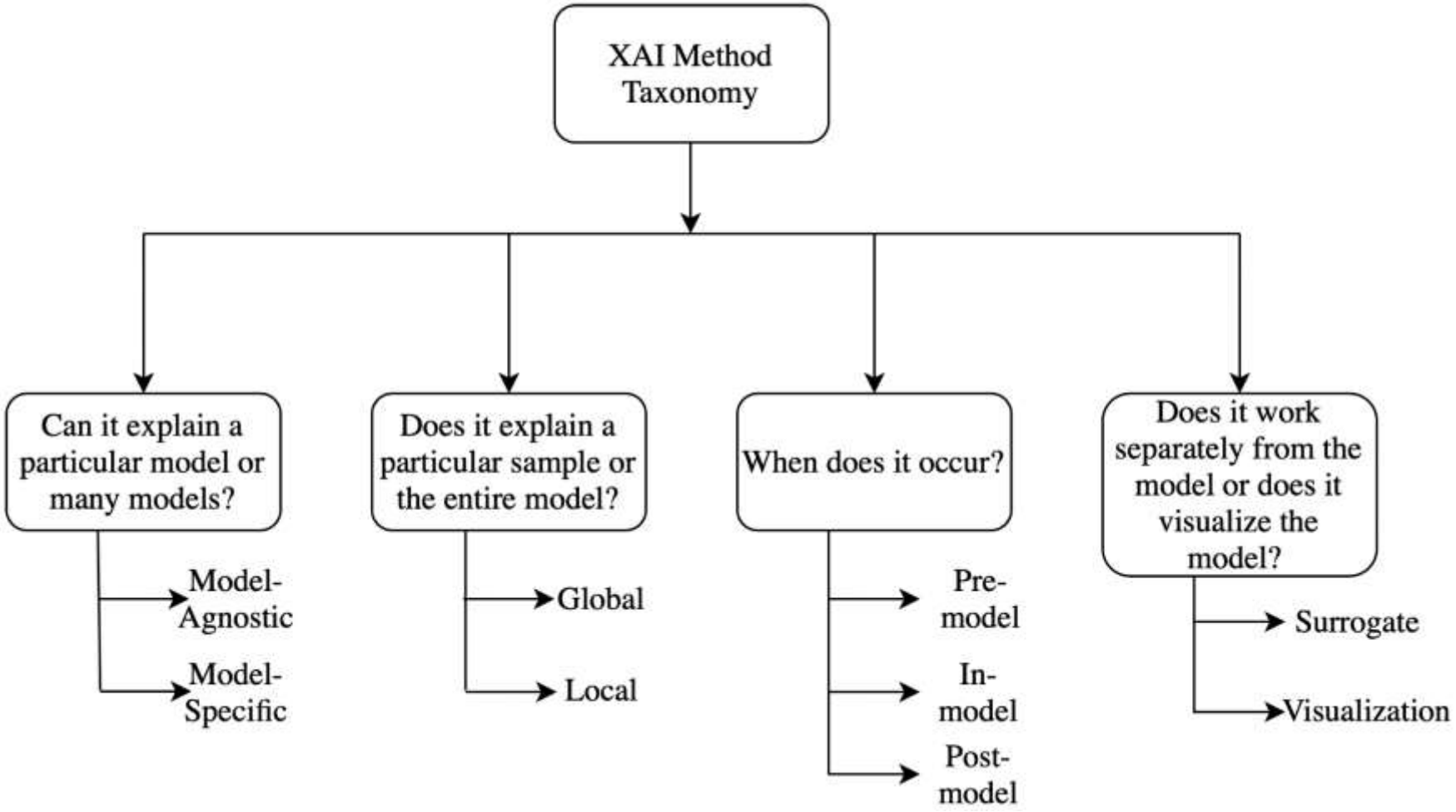
Explainability Taxonomy

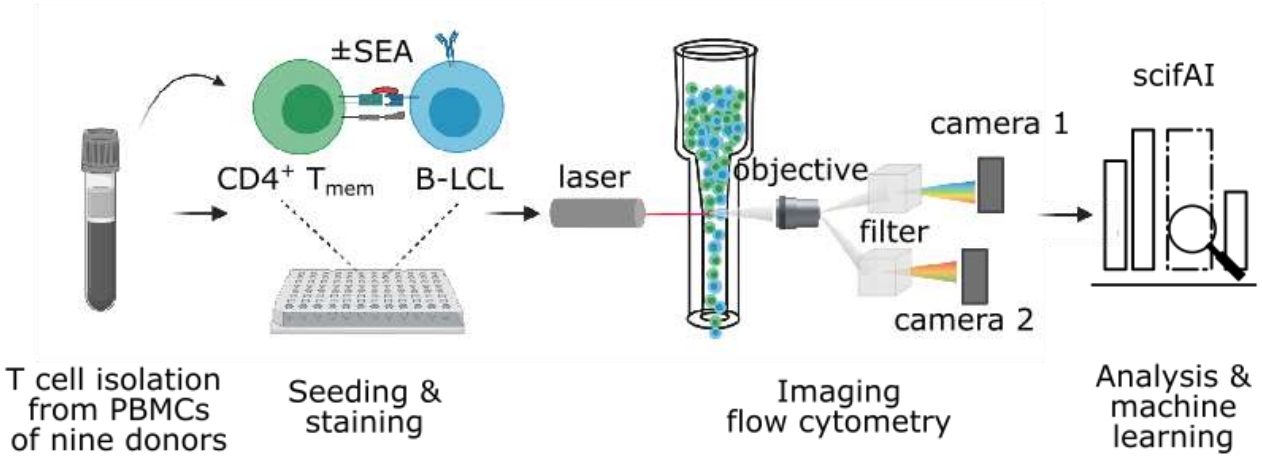


Singh, A.; Sengupta, S.; Lakshminarayanan, V. Explainable Deep Learning Models in Medical Image Analysis. *J. Imaging* **2020**, *6*, 52. https://doi.org/10.3390/jimaging6060052

Part 2: application in antibody screening

Use-case

scifAI: Explainable machine learning for profiling the immunological synapse and functional characterization of therapeutic antibodies



Motivation

- The formation of an immunological synapse is the first event of an adaptive immune reaction between a T cell and an antigen-presenting cell

- **However the mechanisms and modulations by antibodies are still often unclear**

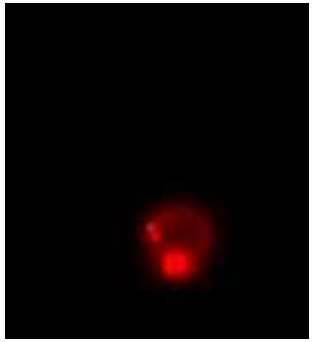
- So far, no study has systematically addressed **how quantity and morphology of the immunological synapse is correlated to T cell function**

- **There is no universal tool for working on imaging flow cytometry data**

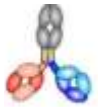
Background

Immunological response

Antigen
Presenting Cell
(APC)

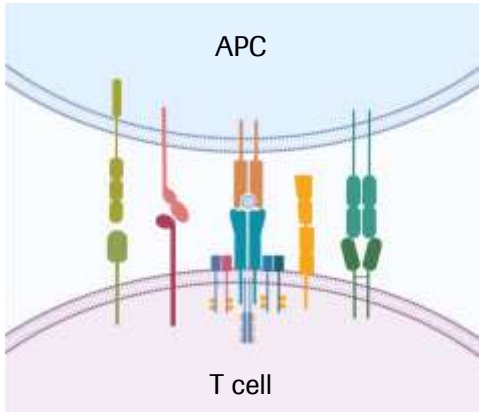


T cell

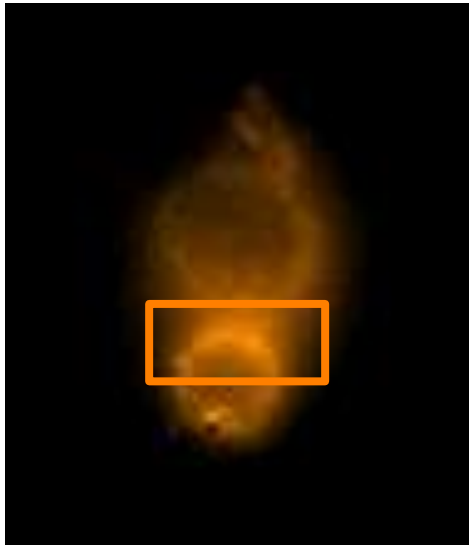


Antibody

Immunological
Synapse
Formation



Formed Synapse



Understand this!

(still quite scientifically unclear)

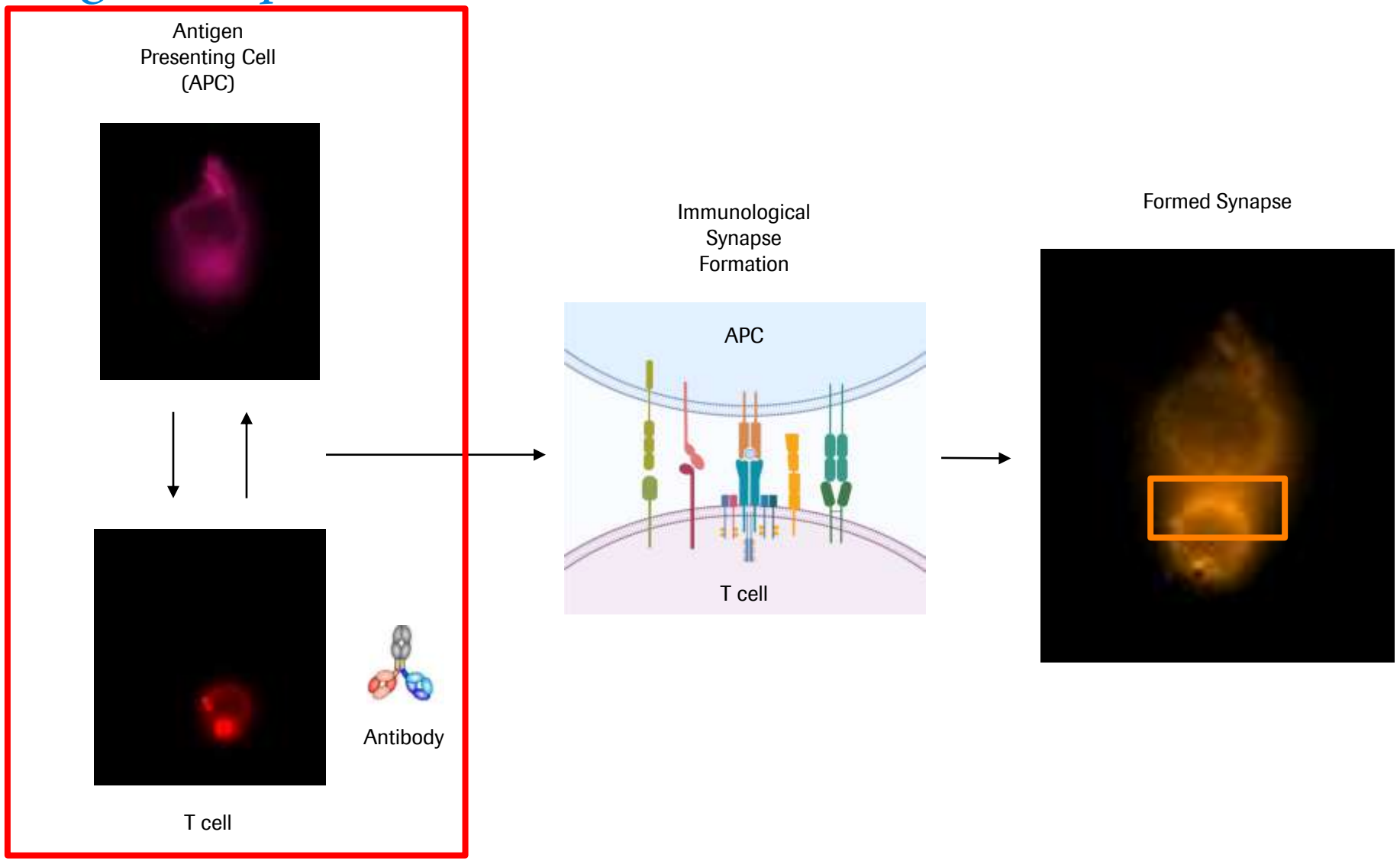
Recording the images

Background

Immunological response

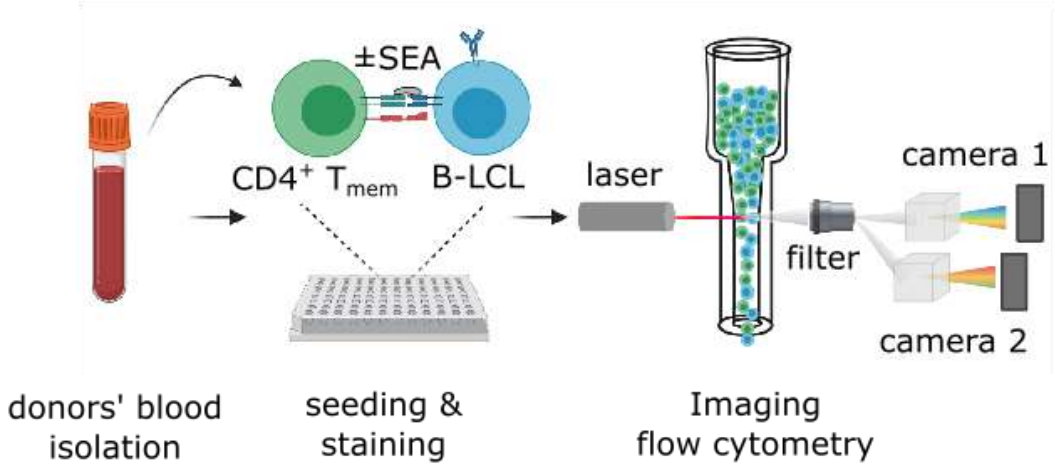
Background

Immunological response

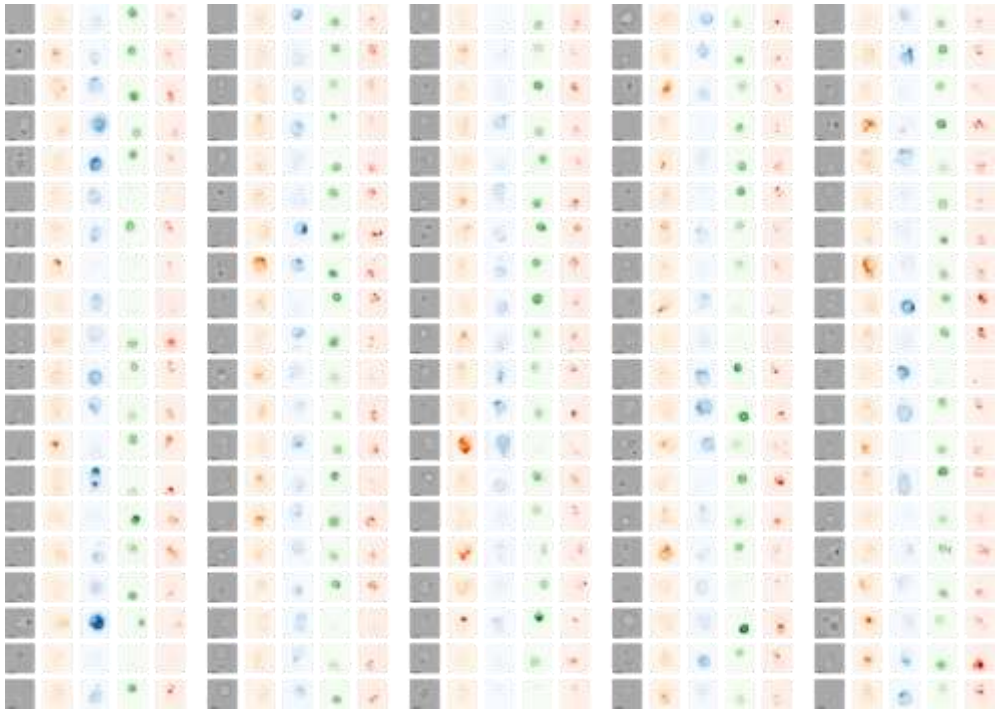


Data Generation Pipeline

Immunological response



Data generation pipeline



More than 3 million images were recorded

Can we classify cell types automatically?

Feature extraction

A modular python package is developed to extract interpretable features

Morphology:
- Shape
- Size
- Roundness
- …

Intensity:
- Mean
- Std
- Shannon entropy
- …

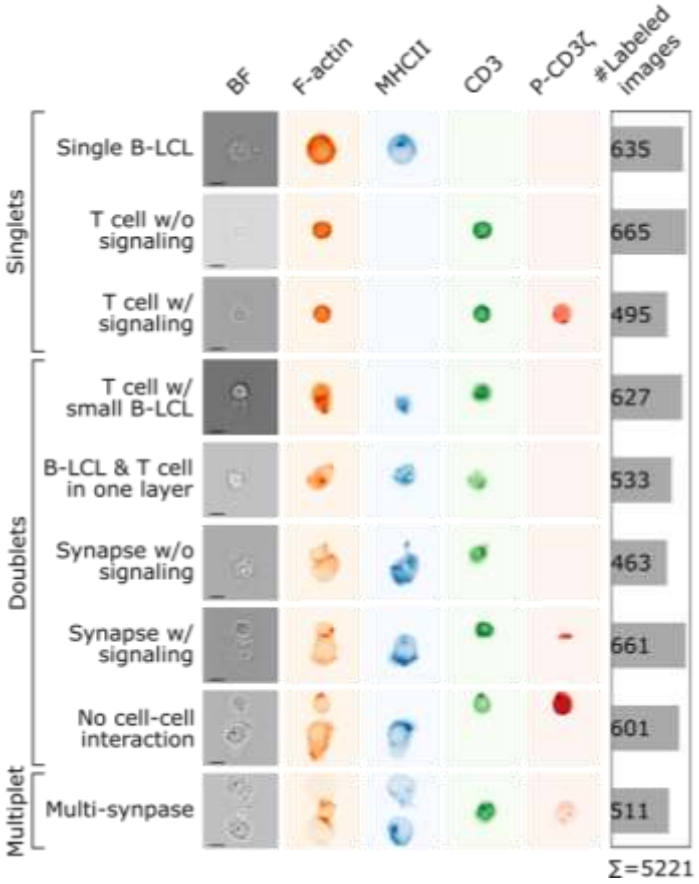
Colocalization:
- Pearson corr.
- Manders Overlap
- Jacquard index
- …

Synaptic features:
- Mean intensity enrichment
- Max intensity enrichment
- …

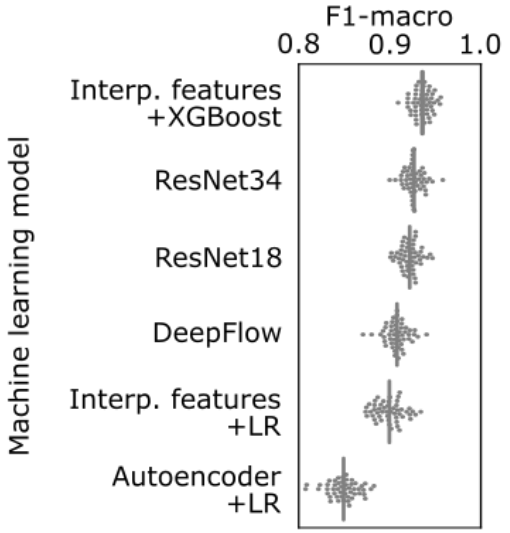
Feature extraction

Explainable machine learning

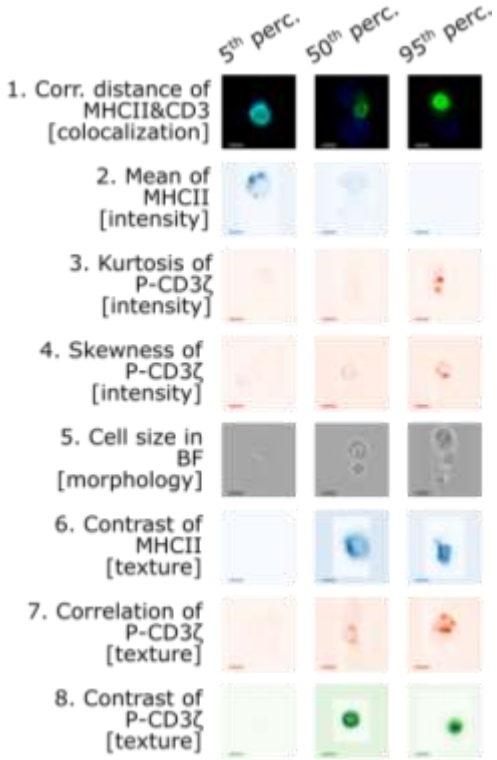
Identification of the most informative image features



Small annotated dataset



Classification

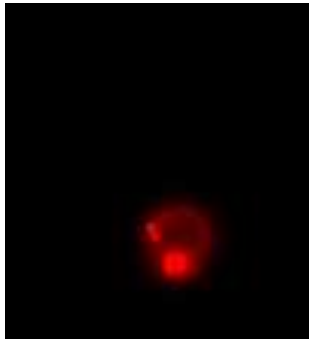


Top features

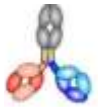
Background

Immunological response

Antigen
Presenting Cell
(APC)

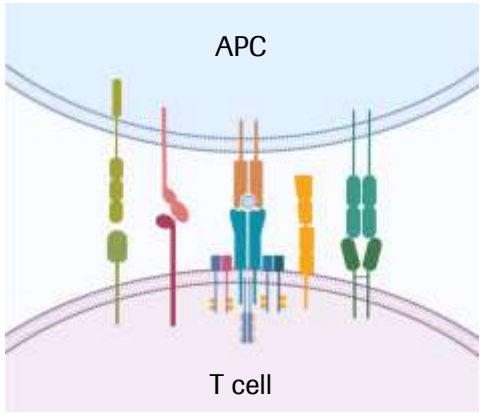


T cell

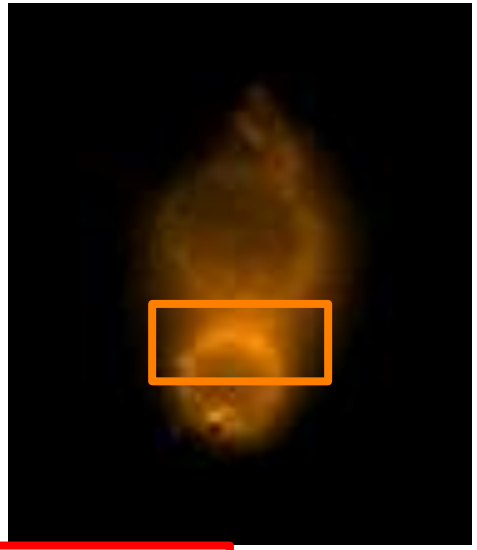


Antibody

Immunological
Synapse
Formation



Formed Synapse



Understand this!

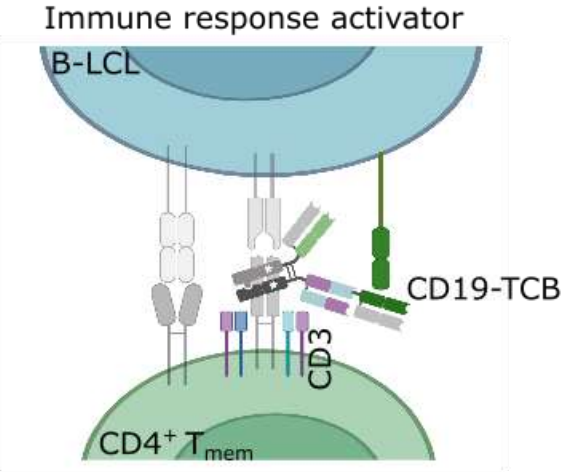
Can we use xAI to profile the mode of action of therapeutic antibodies on synapse formation?

Experimental setup

As a proof of concept, we study an immune response activator

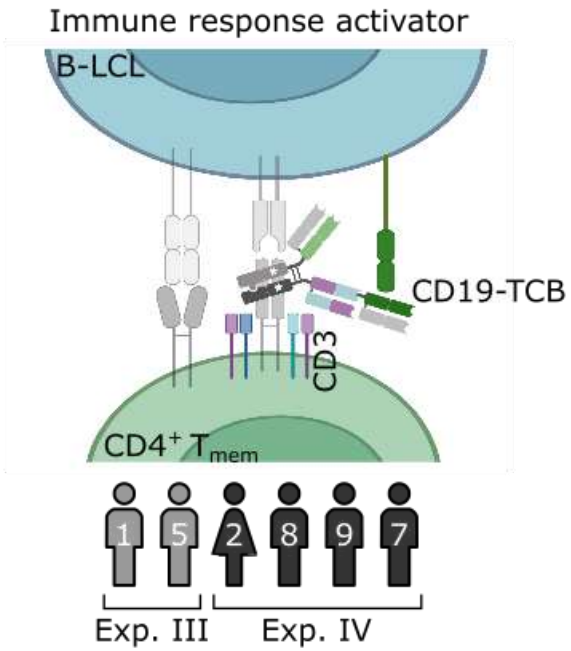
Activator ⟹ B+T cells ⇗ B+T cells + Ctrl

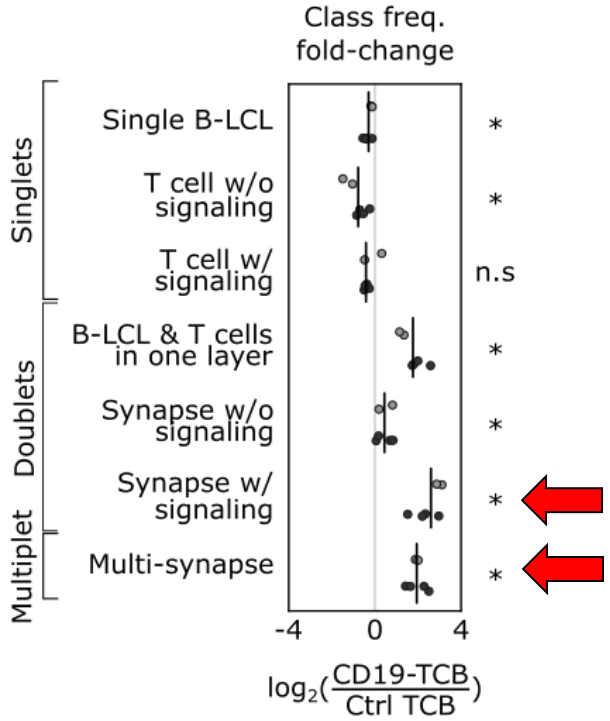
B+T cells ⇘ B+T cells + Ab ↑

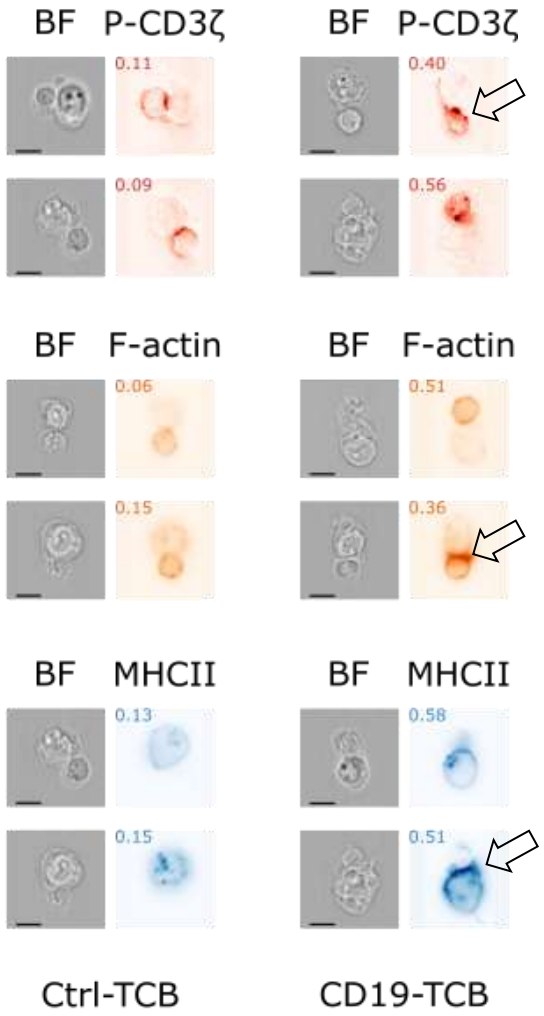


Large therapeutic molecules

Investigating the influence large therapeutic molecules







Summary

- We created an end-to-end pipeline to study immunological synapse
- **xAI allows for studying immunological synapse properties** in an unbiased and systematic way
- **Image-based approach resolves higher order features** of marker expression (e.g. enrichment of MHCII in the synapse of a B/T cell doublets)
- The tool can be used in other IFC datasets and applications.

Doing now what patients need next