# ECLIPSE: A Multivariate Approach for Enhanced Detection of Minimal Residual Disease in Multiple Myeloma Using Multicolour Flow Cytometry

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## Introduction

Minimal Residual Disease (MRD) detection in hematological malignancies like Multiple Myeloma (MM) is vital for treatment evaluation. Manual gating in multicolour flow cytometry (MFC) is subjective and labor-intensive. The percentage of MRD cells is typical low <0.1% Introducing ECLIPSE, an automated multivariate method that enhances MM MRD detection by eliminating normal cells.

**Goal:** systematically find disease-associated cells

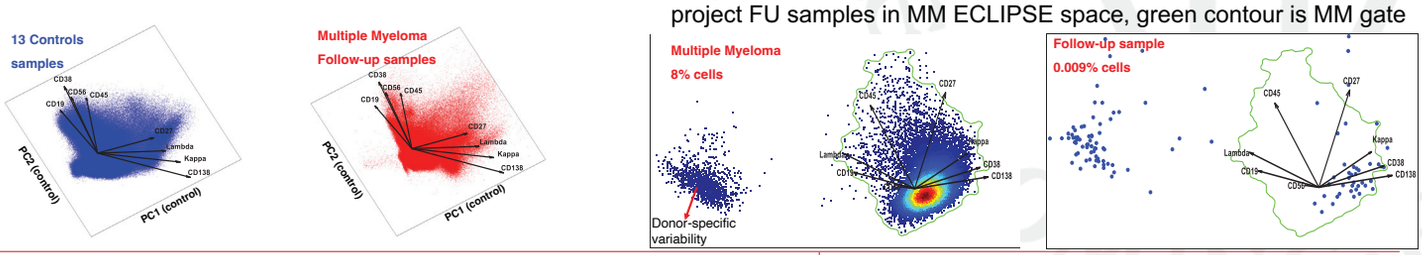
## Methods

ECLIPSE employs an automated elimination step for normal cells in patient samples. Firstly, ECLIPSE uses multiset Simultaneous Component Analysis (SCA) to describe the cell distribution of control bone marrow measurements. Subsequently, the measurements of patient samples at diagnosis and follow-up were projected into the SCA model and the residuals of each cell were calculated. Cells with a low residual error were classified as normal-like and removed, while cells with a high residual error were classified as aberrant and kept.

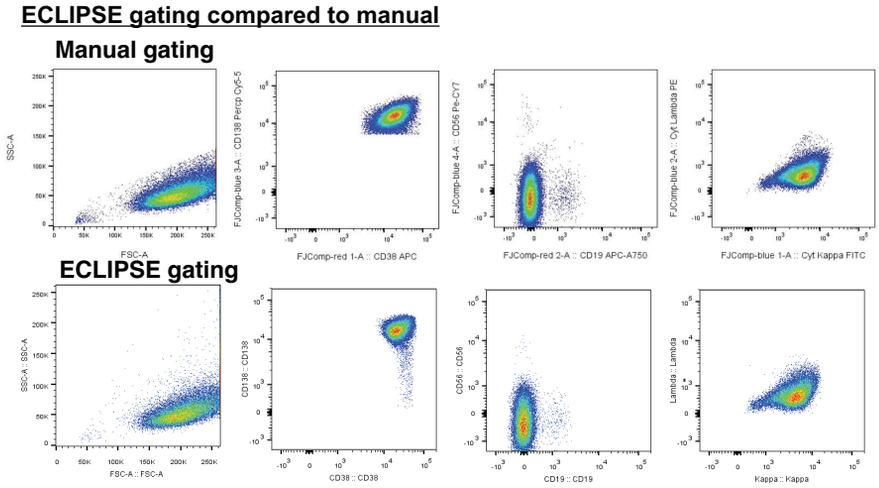
**Step 1:**
SCA of control samples

**Step 2:**
Projection of new samples

**Step 3:**
Keep cells with high residual and perform second SCA on MM samples project FU samples in MM ECLIPSE space, green contour is MM gate



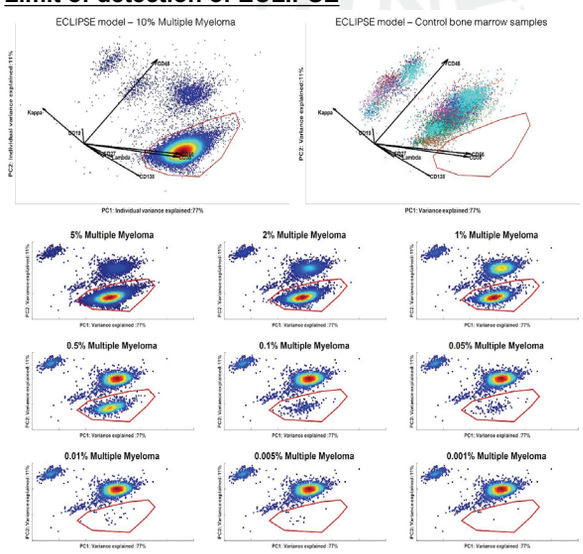

## ECLIPSE gating compared to manual




The ECLIPSE method not only identifies the same cells as manual gating, achieving high recall, but also detects CD138 low cells, thereby enhancing the detectability of MRD.

| % monoclonal plasma cells in ECLIPSE gate | % of cells in ECLIPSE gate overlapping with cells in manual gate | % monoclonal plasma cells in manual gate | Recall | Fold-increase ECLIPSE |
|---|---|---|---|---|
| 0.3 [0.0076 – 0.76] | 0.28 [0.0025 – 0.62] | 0.3 [0.0034 – 0.65] | 0.89 [0.53 – 0.95] | 1.17 [0.93 – 2.24] |

## Limit of detection of ECLIPSE




Samples spiked with cells were projected using the diagnosis-specific model within the ECLIPSE framework, after eliminating normal cells. A gate specific to multiple myeloma was then employed to isolate the spiked monoclonal cells at various proportions, spanning from 5% down to 0.001%.

## Conclusion

ECLIPSE is able to automatically detect MRD cells
~ **2 minutes** computational time for the analysis on the entire dataset (~ 8 000 000 events!)
No need of downsampling before the analysis

### References

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