# A Markov Random Fields approach to the gating of flow cytometry data

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## Introduction

## Flow cytometry is a technology that simultaneously measures and analyses multiple physical and chemical characteristics of single cells as they flow in a stream through a beam of laser light. This technology has become an emerging state-of-the-art device in microbiology and dairy science, and is also used extensively in medical diagnostics. The gating stage of analysis, the identification of homogeneous cell populations, is performed using expert opinion rather than by employing a unified statistical framework. The increased volume and complexity of flow cytometry data resulting from advances in the technology greatly boosts the demand for reliable statistical methods and accompanying software implementations for analysis. The objective of this research is to provide a statistically robust methodology for the gating of flow cytometry data which moves beyond the expert-driven approach currently employed.

**Methodology**

One aspect of flow cytometry data which has not been properly exploited until now is the integer valued nature of such data, resulting from the technology used to record it. Given this structural layer of flow cytometry data each pair of recorded variables can be visualised as a 2-dimensional image. Markov Random Fields (MRF) have been used extensively for image modelling and in recent years for drawing inferences from images [1]. The approach here is to utilise this structure by applying an MRF approach to allow the constructed images to be segmented into regions, each containing a unique sub-population of the recorded cells. MRF also provide a probabilistic foundation to the grid on which the flow cytometry data lies in, allowing additional inferences to be drawn from the image data.

**Results**

The methodology is applied to the rituximab flow cytometry data [2] which appears frequently throughout the flow cytometry literature for the purpose of demonstrating statistical methods on flow cytometry data. The results provide a visual and statistical comparison of the sub-populations identified utilising the current expert-driven approach and the new statistical approach proposed earlier.

**Conclusions & Further Work**

The proposed methodology moves beyond the current industry standard and will aid in the deployment of this state-of-the-art technology to other fields of science and industry. While this research has focused solely on pairwise analysis of variables, which is in line with current industry practices, the future of this project is to expand to a *p*-dimensional setting.

[1] A. Blake, P. Kohli, and C. Rother, *Markov Random Fields for vision and image processing*, MIT Press, Massachusetts, 2011.

[2] M. Gasparetto, T. Gentry, et al., “Identification of compounds that enhance the anti-lymphoma activity of rituximab using flow cytometric high-content screening.”, *Journal of Immunology Methods*, **292**(1), 2004, pp. 59-71.