Estimation of cell-to-cell regulatory heterogeneities from cell populations

Even when appearing perfectly homogeneous on a morphological basis, tissues can be substantially heterogeneous in single-cell molecular expression. Such heterogeneities might govern the regulation of cell fate, and hence one is interested in their quantification in a given tissue. This is typically done given single-cell gene expression data. However, such data is expensive and subject to high technical noise. Hence, in this project we refrain from single-cell data; instead, small numbers of cells are randomly selected, and the subpopulation average expression level is measured. I will discuss how heterogeneities can be detected from such data by application of statistical methods, and how the proportions, mean values and standard deviations of the groups of different cells can be estimated. The estimation techniques are applied to measurements of human breast epithelial cells, showing remarkable agreement with experimental results. Importantly, population-level inference turns out to be much more accurate with pooled samples than with one-cell samples when the extent of sampling is limited.