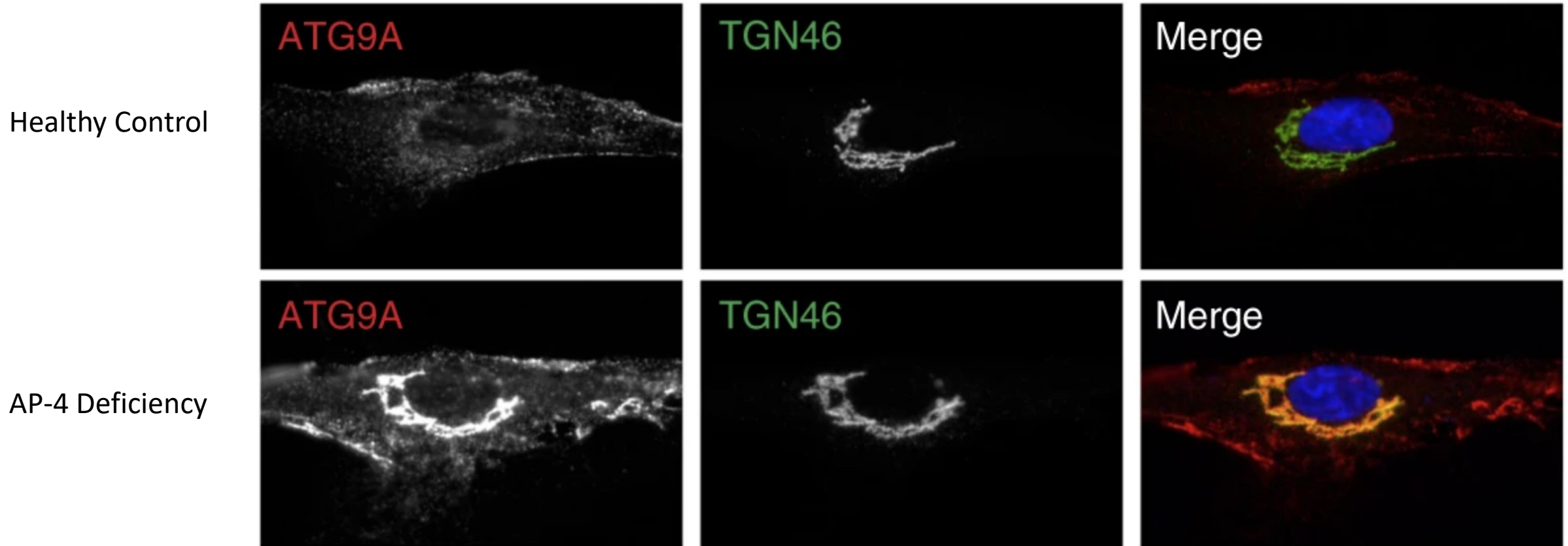


Uncertainty quantification for dynamic spatial proteomic experiments

European Bioconductor conference 2019

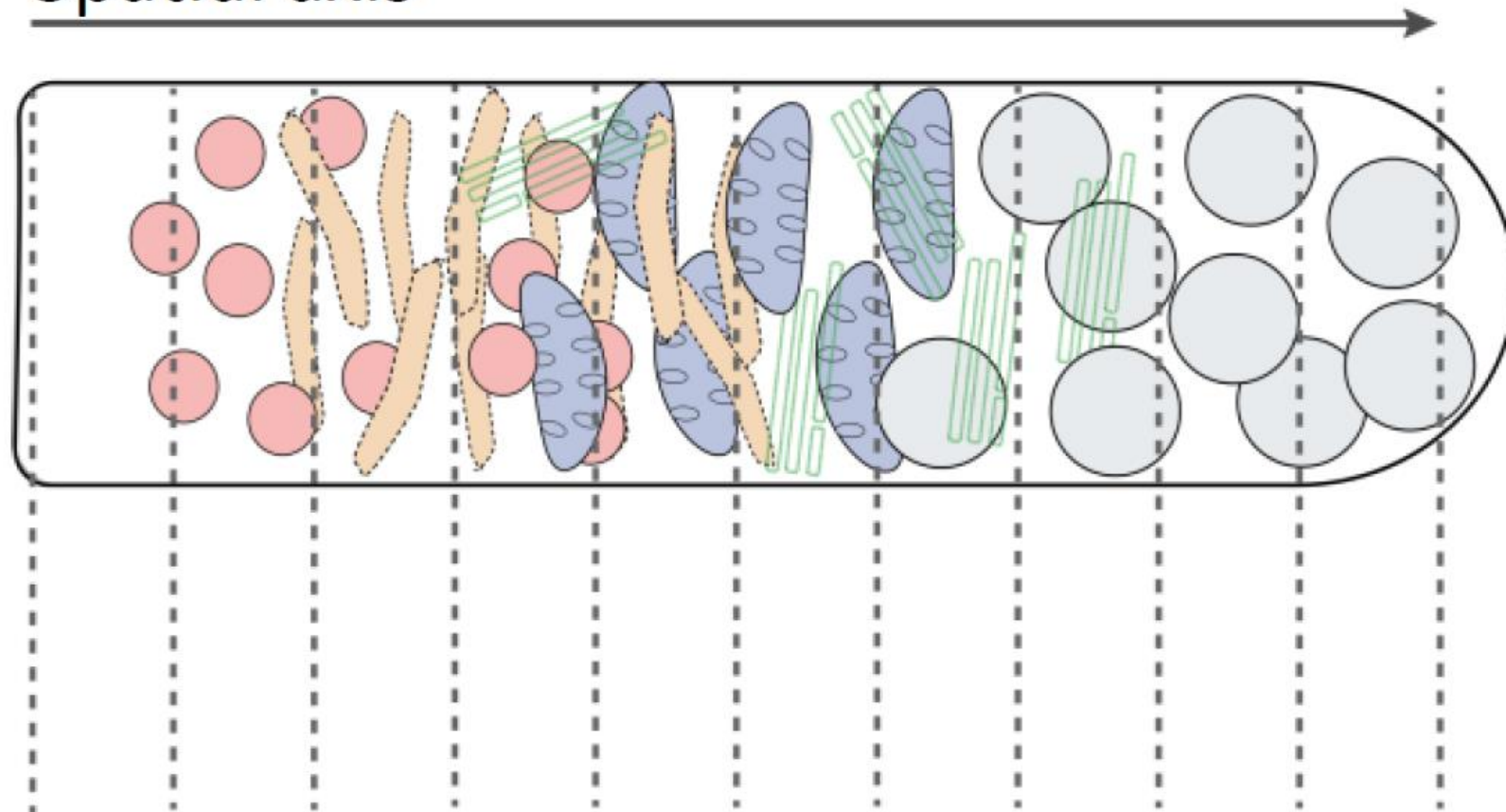
Mis-localisation is phenotypic in AP-4 deficiency syndrome



Density Gradient Separation

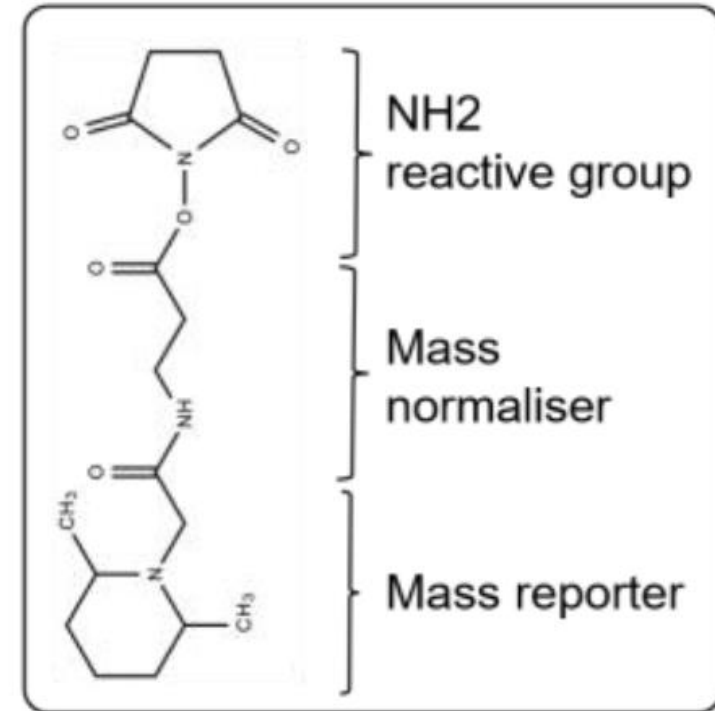
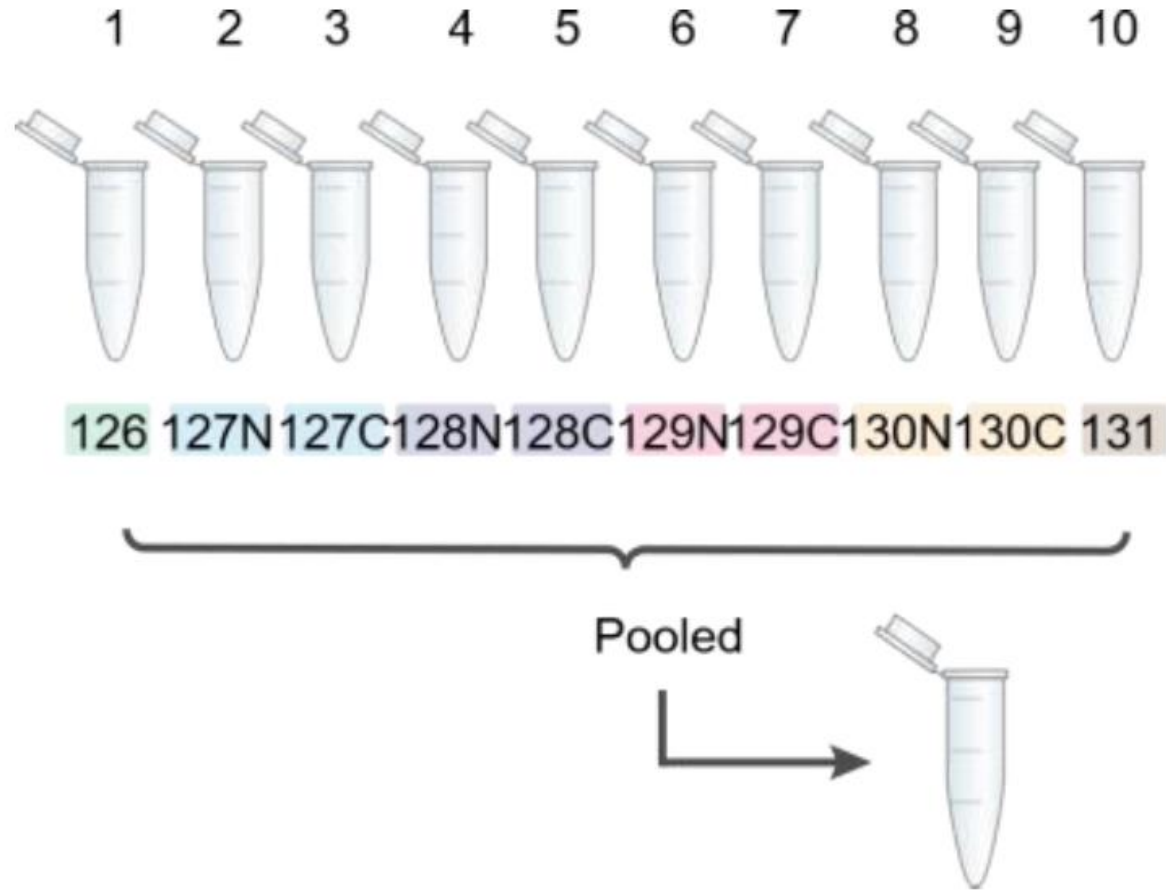
Organelles separated along iodixanol density gradient

Spatial axis



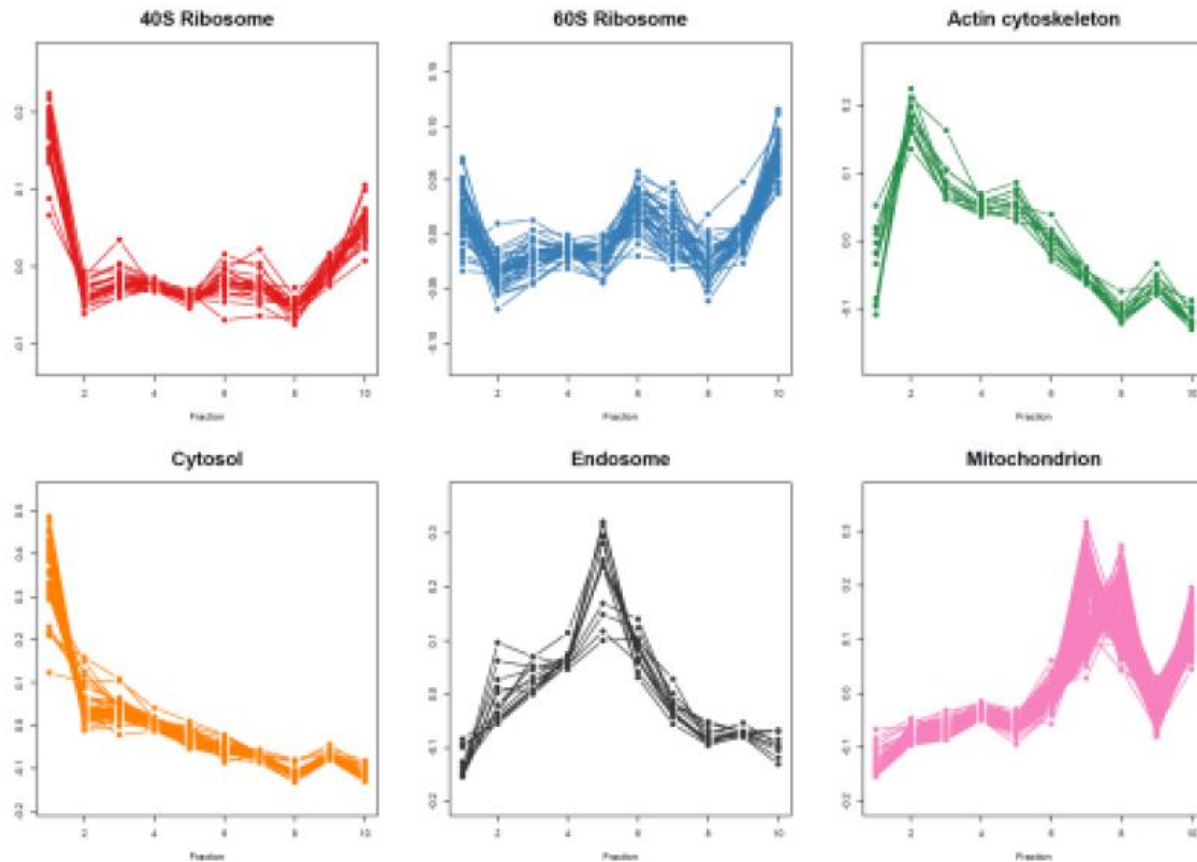
TMT Labelling

Isobaric mass tag labelling of individual fractions



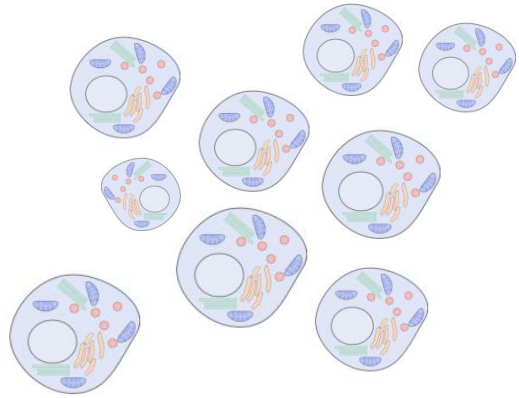
Quantitative Mass-Spectrometry

Complex digest fractionated by high-PH UPLC and analysed by LC/LC SPS-MS3

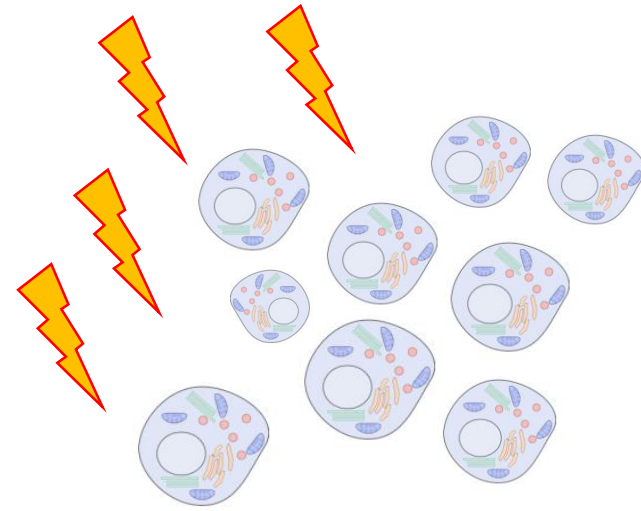


Unique functional profiles for each subcellular niche observed

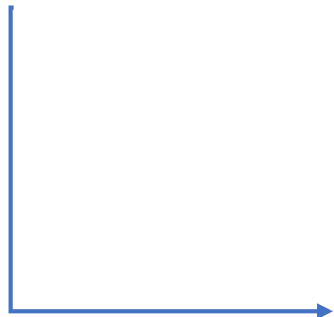
Dynamic spatial proteomics workflow



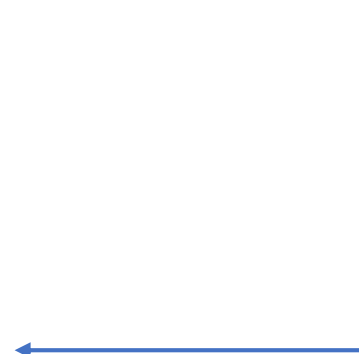
Normal cell population



Perturbed cell population

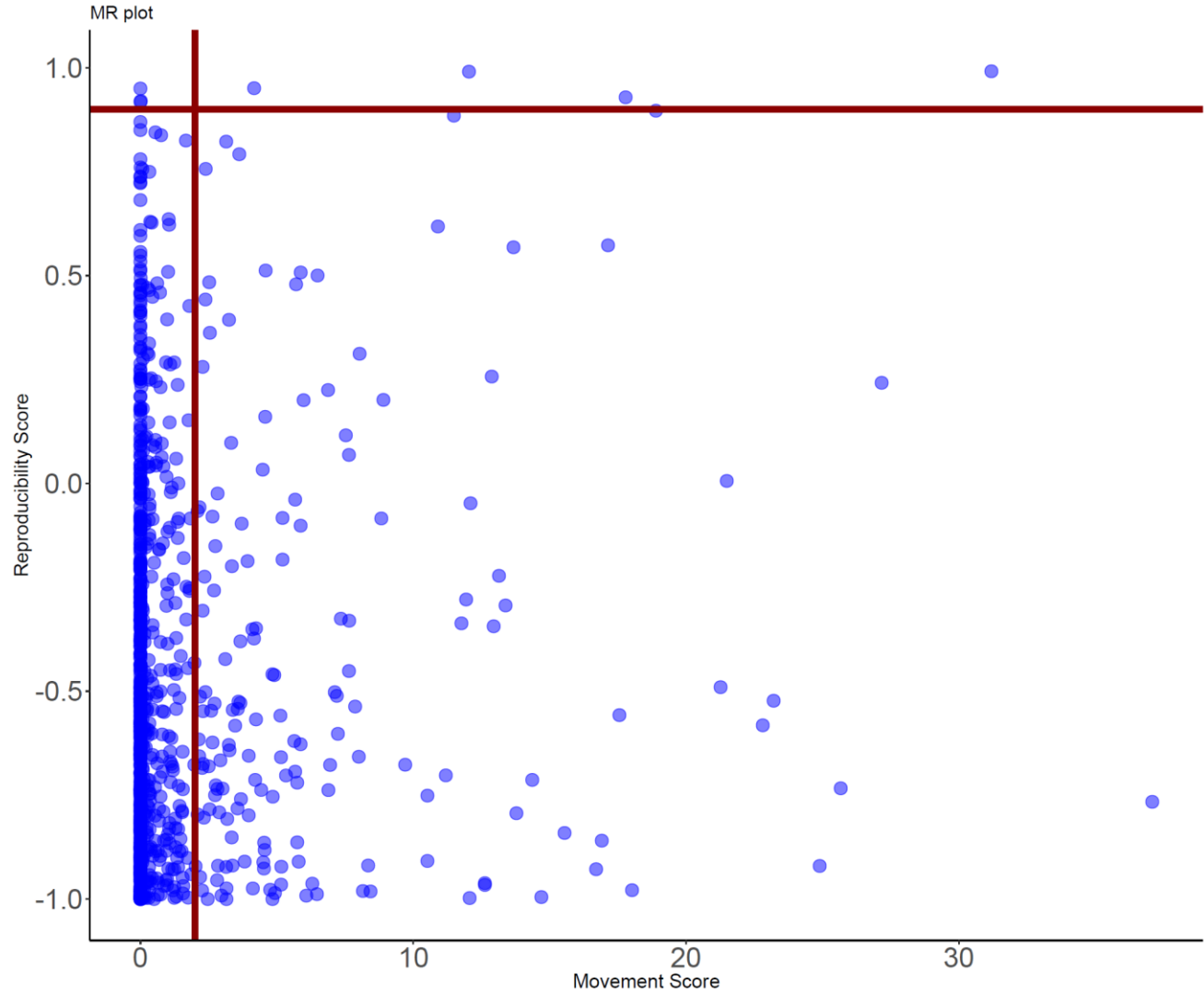


Parallel mass-spectrometry workflow



What proteins re-localise upon perturbation of the subcellular environment?

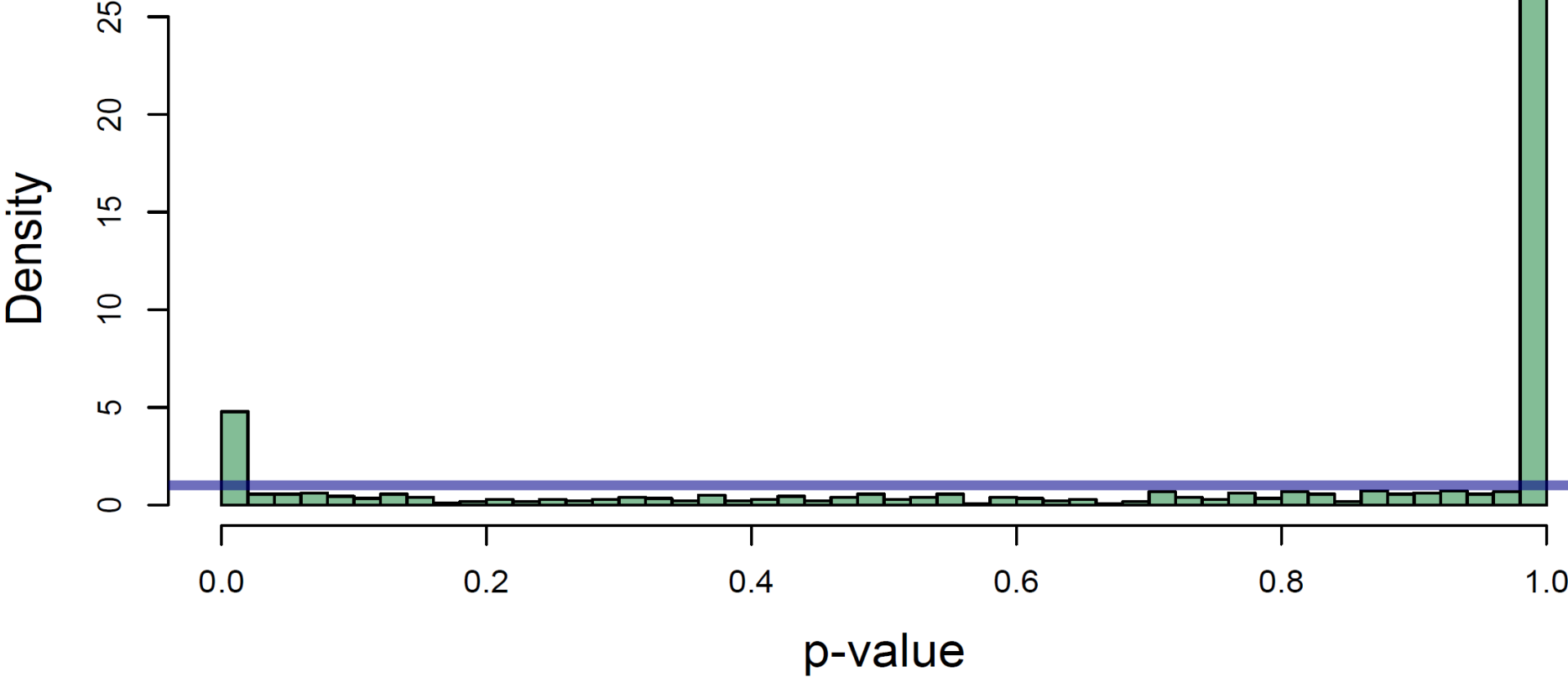
Differential Localisation



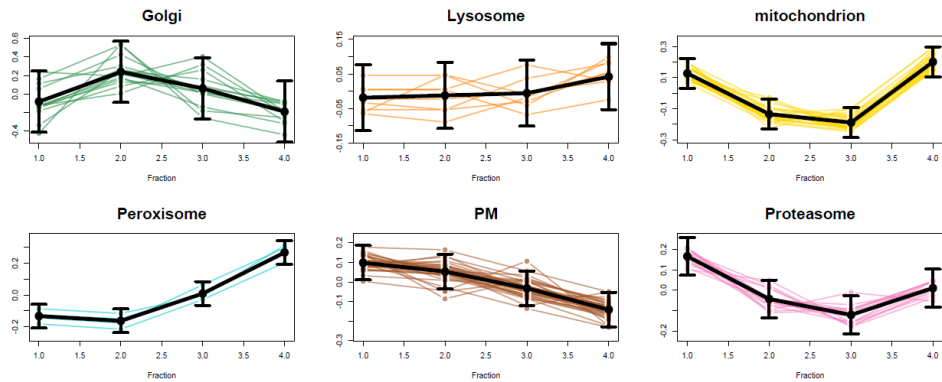
Pearson
Correlation

Chi-Squared test

Histogram of p-values



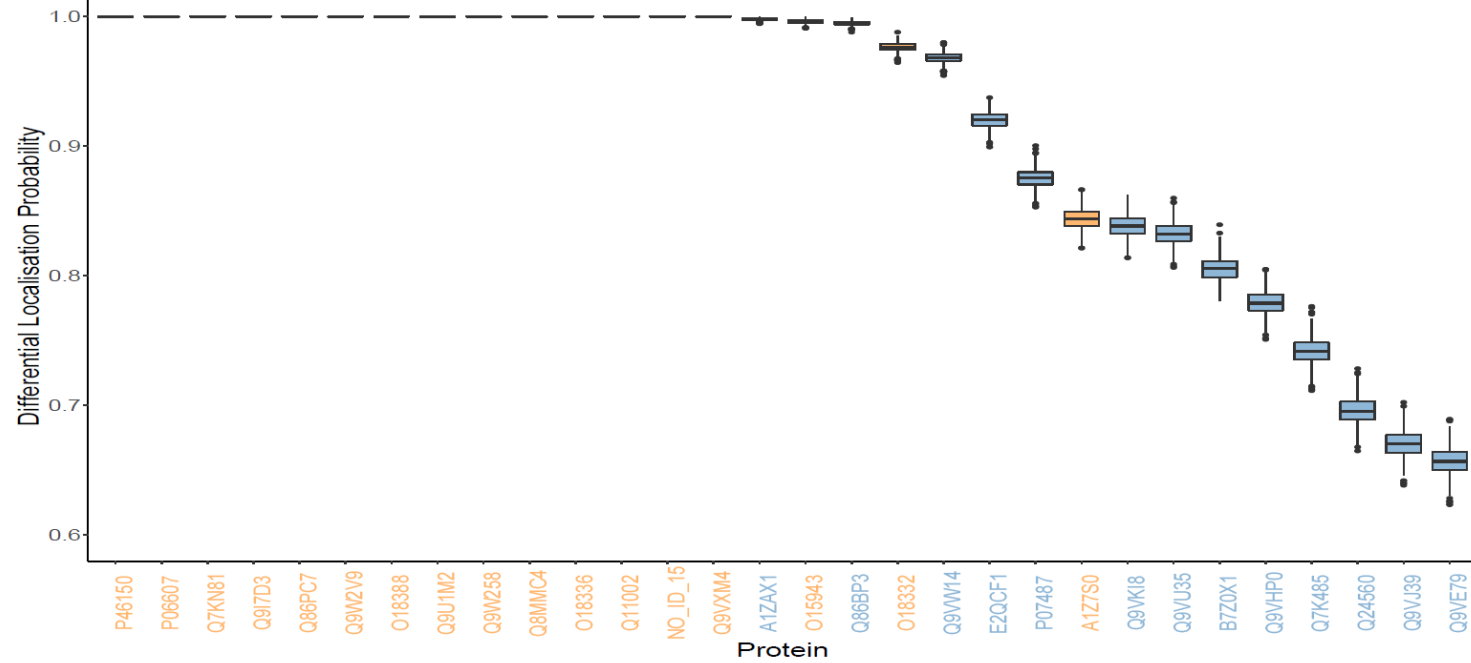
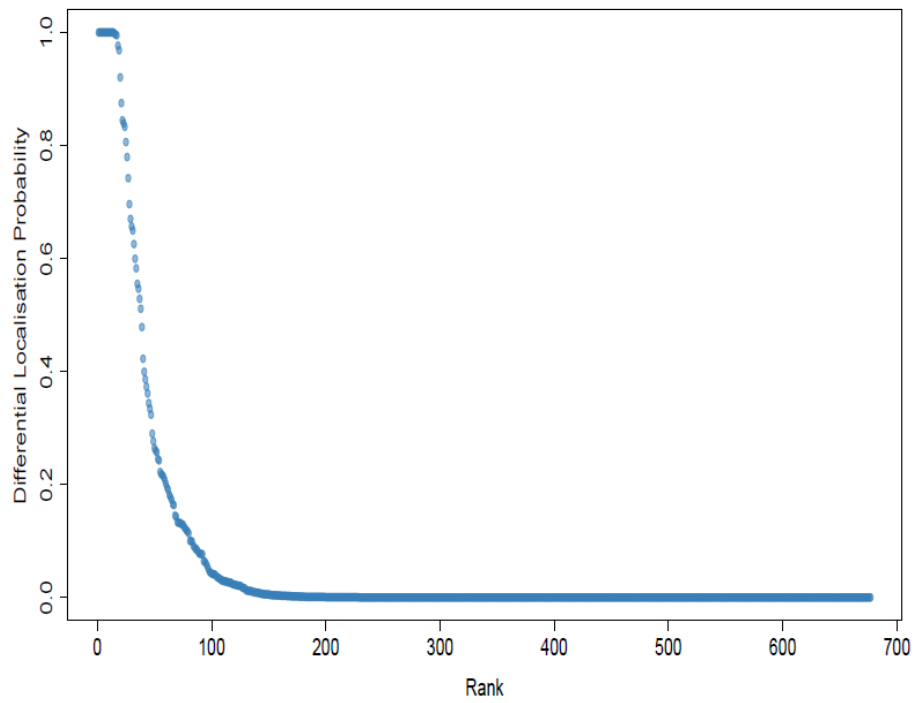
Non-parametric model

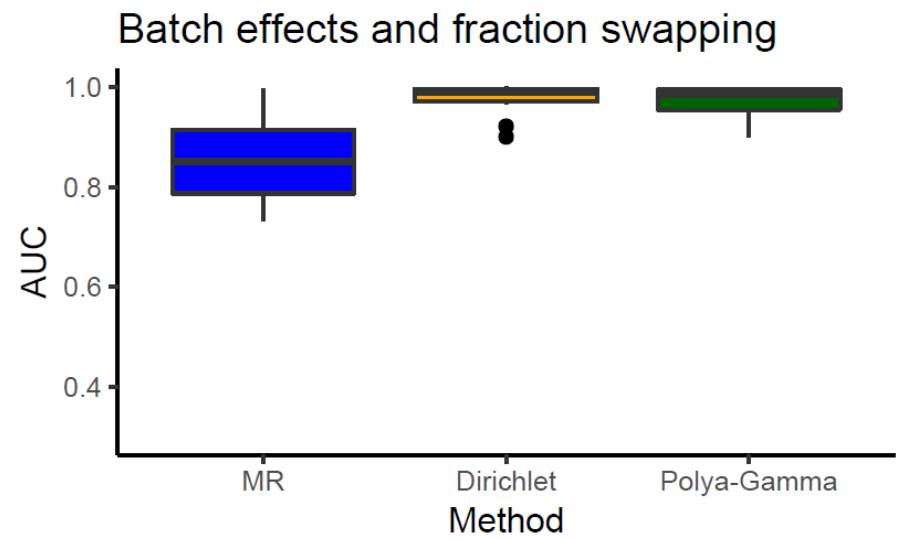
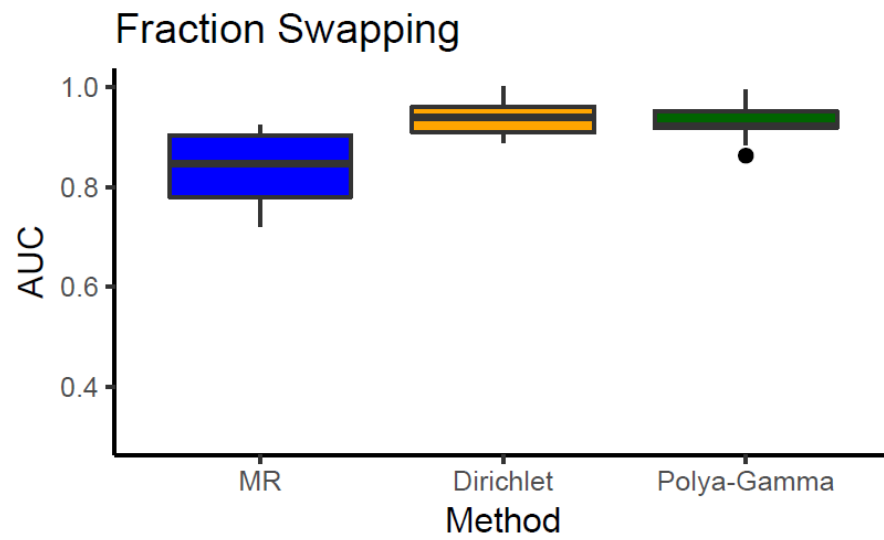
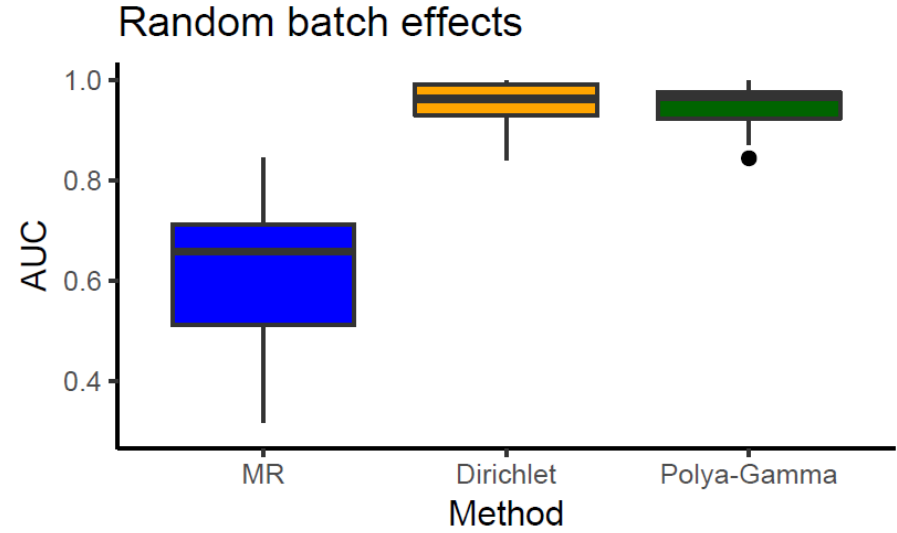
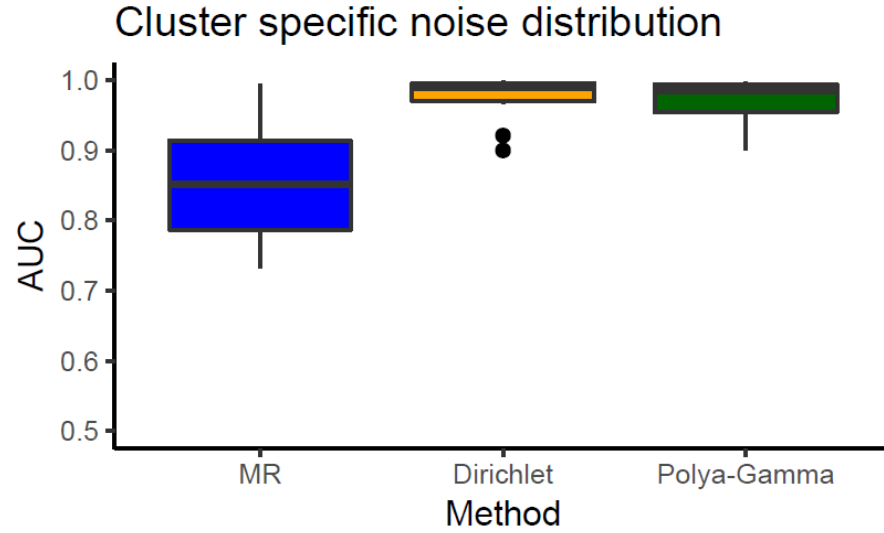


+
$$\left. \begin{aligned} \boldsymbol{\pi} | \boldsymbol{\alpha} &\sim \mathcal{M}\text{Dir}(\boldsymbol{\alpha}, K) \\ (z_{i,1}, z_{i,2}) &\sim \text{cat}(\boldsymbol{\pi}), \end{aligned} \right\} \text{Conjugate prior}$$

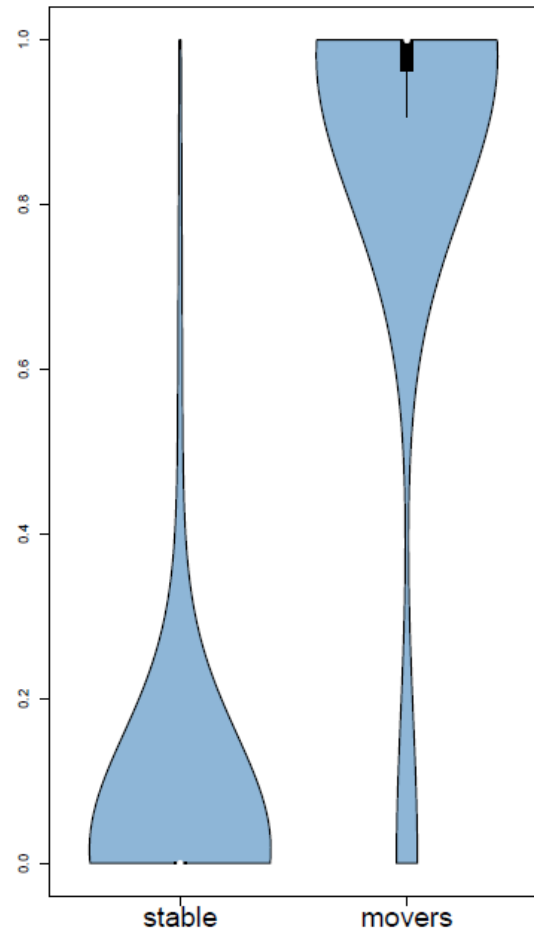
Joint allocation for protein i across datasets

Allows us to calculate the probability that a protein is differentially localisation

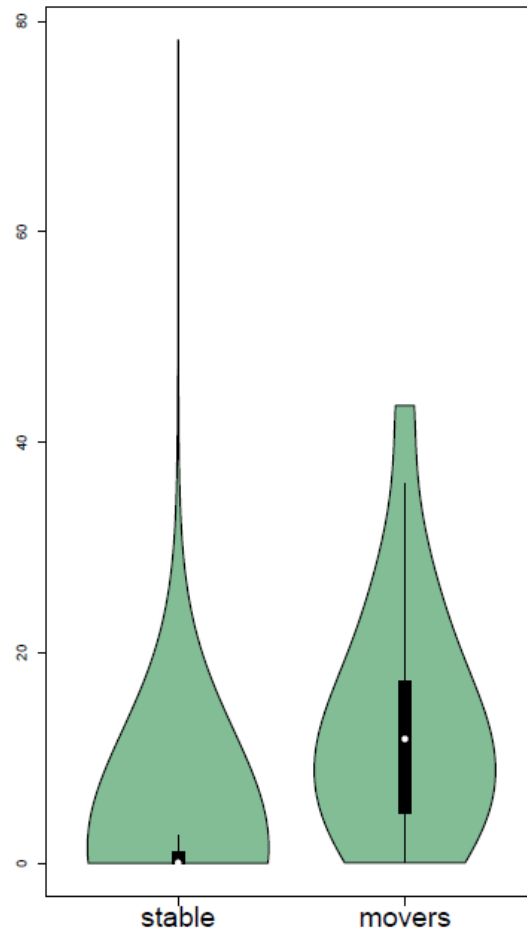


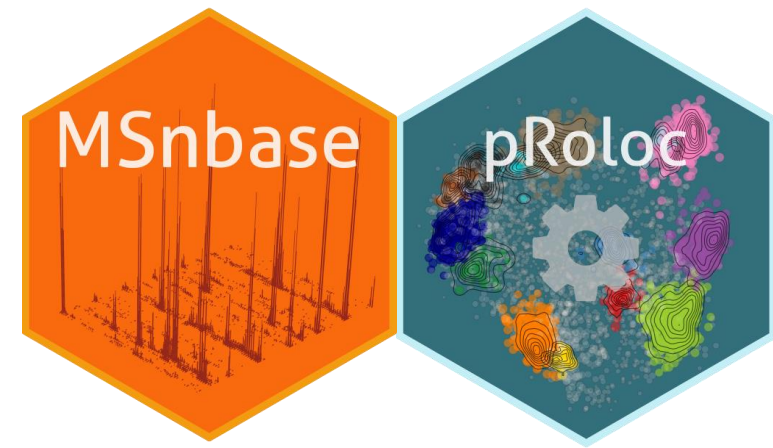


Differential localisation Probabilities



M Score





Thank You