

# Mathematical Frameworks for Integrative Analysis of Multi-omics Biological Data

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## **Abstract**

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## **Introduction to single cell and imaging multi-omics**

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## **Current multi-omic technologies**

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## **Challenges for interpretation**

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Need for technology-specific questions and analysis methods vs one size fits all data blender

## **Case studies**

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### **scNMT-seq as a case-study for epigenetic regulation**

#### **Overview and biological question**

#### **Computational challenges**

- Identification of multi-omics signatures that characterise lineage, stage or both.
- Handling missing values
- Do epigenetic changes in some genomic contexts affect cell fate decision more than others? If so, how?

#### **Methods for stats/maths analyses and results summary**

### **scRNA-seq + FISH as a case study for spatial transcriptomics**

#### **Overview and biological question**

#### **Computational challenges**

- Can scRNA-seq data be overlaid onto seqFISH for resolution enhancement
- What is the minimal number of genes needed for data integration?
- Are there signatures of cellular co-localization or spatial coordinates in the non-spatial scRNA-seq data?

#### **Methods for stats/maths analyses and results summary**

### **Spatial proteomics and cross-study analysis**

#### **Overview and biological question**

#### **Computational challenges**

- Integrating partially-overlapping proteomic data collected on different patients with similar phenotypes
- Integration of spatial x-y coordinate co-location and co-expression
- Integration with other 'omics datasets (e.g., scRNA-seq) to support the results of these proteomic analyses
- Can we predict the spatial expression patterns of proteins measured on mass-tag but not measured in the MIBI-TOF data?
- What additional information can we learn about the different macrophage and immune populations in breast cancer by conducting integrated analyses of these datasets?

## Methods for stats/math analyses and results summary

## Overview of common analytical methods spanning technologies / case studies

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- matrix factorization
- neural network / autoencoders

## Data structures and software packages to enable analyses

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- Bioc/multiAssayExperiment for single cell
- new classes for proteomics
- PyTorch

## Techniques and challenges for benchmarking methods

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- realistic simulation studies
- cross-validation, issues in matching dimensions of latent space across folds
- cross-study validation
- benchmark datasets

Relevant citations to include as literature review on benchmarking multi-modal methods:

- Fertig 2012 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3460736/>
- Haibe-Kains 2012 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3283537/>
- Meng 2019 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6692785/>
- Pratapa 2020 <https://www.ncbi.nlm.nih.gov/pubmed/31907445>

Other links:

- Levi Waldron's benchmarking repo <https://github.com/waldronlab/awesome-bioinformatics-benchmarks>
- Mike's reviews / evaluation section of `awesome-multi-omics` <https://github.com/mikelove/awesome-multi-omics#multi-omics-reviews--evaluations>

## Discussion

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### Emerging analytical methods and technologies

### Community needs for data structures, analysis methods, etc

# References

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