

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

This manuscript ([permalink](#)) was automatically generated from [BIRSBiointegration/whitePaper@2ba0515](#) on June 22, 2020.

## Authors

---

- **Kim-Anh Lê Cao**

 [0000-0003-3923-1116](#) ·  [mixOmicsTeam](#) ·  [mixOmicsTeam](#)

Melbourne Integrative Genomics, School of Mathematics and Statistics, University of Melbourne, Australia · Funded by Grant National Health and Medical Research Council Career Development fellowship (GNT1159458)

- **Aedin C Culhane**

 [0000-0002-1395-9734](#) ·  [aedin](#) ·  [AedinCulhane](#)

Data Sciences, Dana-Farber Cancer Institute, Boston, MA, USA; Biostatistics, Harvard TH Chan School of Public Health, Boston, MA, USA · Funded by Chan Zuckerberg Initiative, NIH, DoD (need to get grant IDs)

- **Elana Fertig**

 [0000-0003-3204-342X](#) ·  [ejfertig](#) ·  [FertigLab](#)

Department of Oncology, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD, USA; Department of Biomedical Engineering, Johns Hopkins University School of Medicine, Baltimore, MD, USA; Department of Applied Mathematics and Statistics, Johns Hopkins University Whiting School of Engineering, Baltimore, MD, USA · Funded by National Institute of Health, National Cancer Institute; National Institute of Health, National Institute of Dental and Craniofacial Research; Lustgarten Foundation; Emerson Foundation; Allegheny Health Network

- **Jane Roe**

 [XXXX-XXXX-XXXX-XXXX](#) ·  [janeroe \(PLEASE COPY/PASTE DO NOT EDIT THIS ONE\)](#) ·  [XXX](#)

Department of Something, University of Whatever; Department of Whatever, University of Something · Funded by XX

## **Abstract**

---

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

---

## **Current multi-omic technologies**

---

## **Challenges for interpretation**

---

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

## **Case studies**

---

### **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

---

- matrix factorization
- neural network / autoencoders

## Data structures and software packages to enable analyses

---

Basic objectives:

- Support development of efficient data containers/data services, balancing abstraction with concrete responsiveness to new biotechnologies
- Support software developers in achievement of scalability in their tools
- Support end-users in adoption and successful use

## A software ecosystem for multimodal single cell genomics

- Defining the ecosystem; scope and principles of evolution
- Current content targets
  - spatial transcriptomics
  - scNMT-seq ...
- Governance concepts

## Containers for developers and users

## Details of working components

Type	Brief name	Description	URL	Author email
data class	MultiAssayExperiment	unify multiple experiments	biocoductor.org	many
R package	Giotto	Spatial transcriptomics	...	...
python library	PyTorch	deep learning	...	...

## Techniques and challenges for benchmarking methods

---

- 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

---

**Emerging analytical methods and technologies**

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

## Glossary

---

- **Term:** Write the definition as a sentence.

# References

---