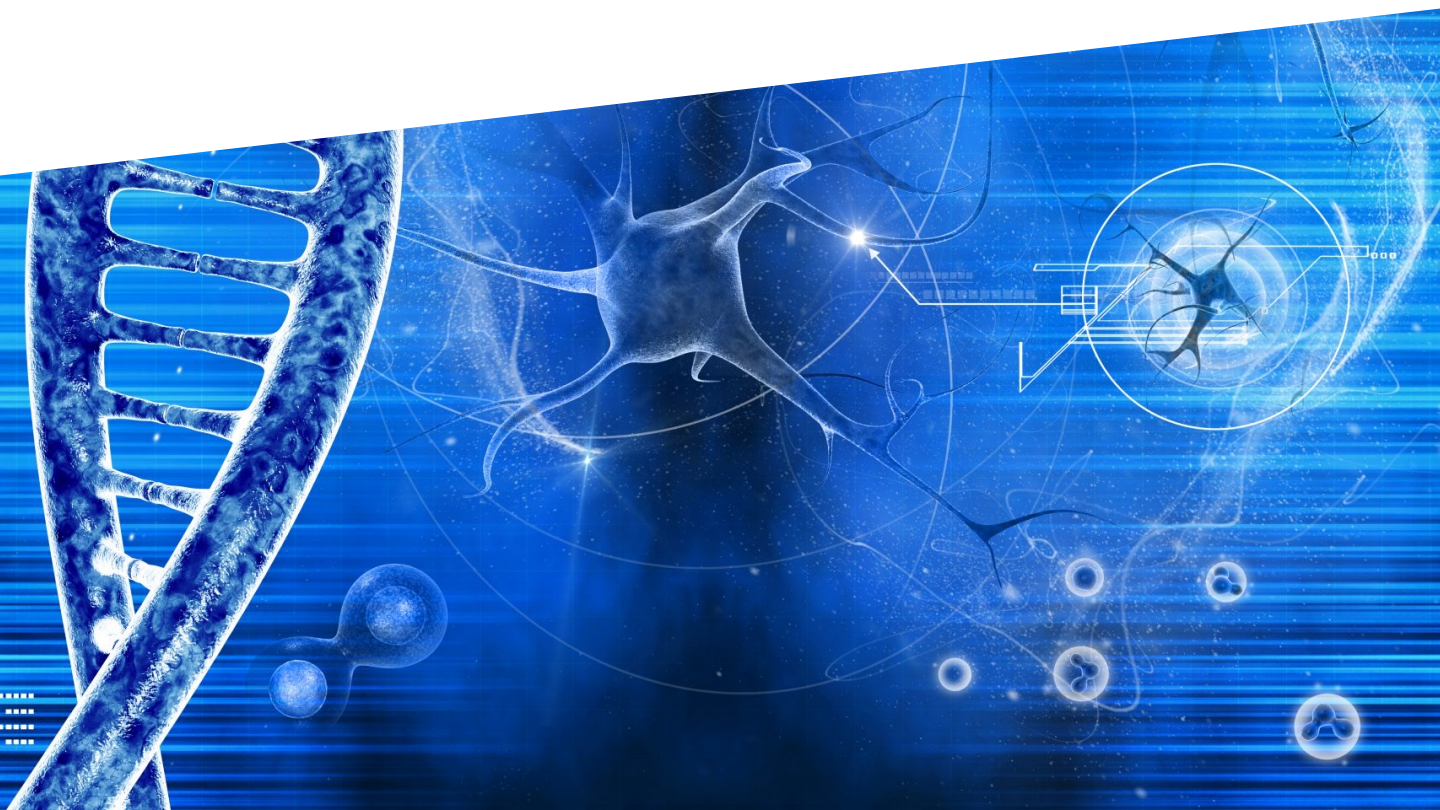
HUMAN TECHNOPOLE

BRAINOMICS

computational approaches to single-cell multi-omics in neuroscience

28 November - 2 December 2022
Human Technopole, Milan (IT)



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FACULTY

Scientific Organisers

- Giuseppe Testa (Head of Research Centre)
- Jose Davila-Velderrain (Group Leader)
- Elena Taverna (Group Leader)

External Speakers and Instructors

- J. Gray Camp (University of Basel, CH)
- Denis Jabaudon (University of Geneva, CH)
- Peter Kharchenko (Atlos Labs, US)
- Gioele La Manno (École Polytechnique Fédérale de Lausanne, CH)
- Shahin Mohammadi (Insitro, US)
- Genevieve Stein-O'Brien (Johns Hopkins University, US)
- Bosiljka Tasic (Allen Institute for Brain Science, US)
- Joshua Welch (University of Michigan, US)

HT Speakers and Instructors – Neurogenomics Research Centre

- Daniele Capocefalo (Postdoc)
- Nicolò Caporale (Postdoc)
- Davide Castaldi (PhD Student)
- Cristina Cheroni (Postdoc)
- Elena Taverna (Group Leader)
- Giuseppe Testa (Head of Research Centre)
- Jose Davila-Velderrain (Group Leader)
- Emanuele Villa (Staff Scientist)
- Alessandro Vitriolo (Postdoc)
- Asia Zonca (PhD Student)

FACULTY

HT Facilities and Support Units

- Genomics Technologies Development Unit, Genomics Research Centre (Nicola Crosetto, Senior Manager)
- Automated Stem Cell and Organoid Facility (Giovanni Faga, Head)
- Image Analysis Facility (Florian Jug, Head)
- Light Imaging Facility (Nicola Maghelli, Senior Manager)
- Genomics Facility (Clelia Peano, Senior Manager)
- Electrophysiology Scientific Service, Neurogenomics Research Centre (Diletta Pozzi, Manager)

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CONCEPT

Course Overview

Single-cell omics technologies are breaking new ground in neurobiology by substantially increasing the precision and resolution with which the complex cell populations of the nervous system can be characterised. Approaches that profile several layers of information (genome, epigenome, transcriptome, proteome) allow to generate data of unprecedented depth on the molecular state of the diversity of cells composing the nervous system.

This increase in data volume and complexity generates as many opportunities as new analytical challenges.

This compact course aims at empowering participants in mastering key computational tools for the analysis of single cell multi-omics datasets, starting from individual molecular layers to then tackle their integration, alongside providing a theoretical overview of the impact of these technologies at the leading edge of neurobiology.

Target Audience

This course is aimed at bioinformaticians and computational biologists with (at least) a basic knowledge of omics techniques.

The core of the course will be centred around hands-on data analysis sessions. A basic understanding of Unix command line, python and/or R is required. Previous experience with single-cell analytical workflow will be considered as an added value to harness the most from the course structure.

Main Topics

Lectures: impact of multimodal approaches on neurobiology research; innovative computational approaches for multi-omics data analysis and integration.

Computational hand-on sessions: key steps and troubleshooting in the analysis of single-cell transcriptomics data; multiplexing approaches and demultiplexing algorithms; analytical workflow for single cell ATACSeq; multi-omics data integration.

Wet Lab demo session: technologies for multimodal single-cell interrogation in neural tissues.

Roundtable with core facilities: structuring integrated multi-omic/functional workflows for neural tissue.

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(time in CET, UTC +1)

PROGRAMME

DAY 1

Monday 28 November 2022

09.00 – 09.30	Meet + Greets + Coffee
	LECTURES: Impact of multi-omics approaches on neurobiology
09:30 – 10:20	(40′ talk + 10′ discussion) [Giuseppe Testa]
10.20 – 11.10	(40′ talk + 10′ discussion) [J. Gray Camp]
11.10 – 11.30	**COFFEE**
11.30 – 12.20	(40′ talk + 10′ discussion) [Bosiljka Tasic]
12:20 – 13:10	(40′ talk + 10′ discussion) [Peter Kharchenko]
13:10 – 14:00	**LUNCH**
14.00 – 18.00	HANDS-ON COMPUTATIONAL: Experimental design and multiplexing
(with breaks)	approaches in single-cell transcriptomics
	[Emanuele Villa, Davide Castaldi, Cristina Cheroni, Nicolò Caporale]
	• Key aspects in the experimental design and analytical approaches of single-cell transcriptomics
	• Multiplexing strategies: genetic multiplexing and lipid-tagged indices
	• Demultiplexing algorithms and pipelines

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PROGRAMME

DAY 2

Tuesday 29 November 2022

	LECTURES: Charting the molecular complexity of brain cells
09:30 – 10:20	(40′ talk + 10′ discussion) [Denis Jabaudon]
10.20 – 10.50	**COFFEE**
10.50 – 11.40	(40′ talk + 10′ discussion) [Gioele La Manno]
11.40 – 12.30	(40′ talk + 10′ discussion) [Elena Taverna]
12.30 – 14.00	**LUNCH**
14.00 – 16.00	HANDS-ON COMPUTATIONAL: Key steps and troubleshooting in the analysis of single-cell transcriptomics data [Emanuele Villa, Cristina Cheroni, Nicolò Caporale] • QCs and filtering steps; feature selection and normalization • Dimensionality reduction, clustering and population annotation • Pseudotime-related algorithms and trajectory inference • Data integration: pros and cons
16:00 – 16:30	**COFFEE**
16:30 – 18:30	Studying the complexity of brain cells: a glimpse at the benchwork • Group A: Round table and facilities tour «Structuring integrated multi-omic/functional workflows for neural tissue» • Group B: Robotics for multimodal single cell phenotyping in the developing brain [Elena Taverna]

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PROGRAMME

DAY 3

Wednesday 30 November 2022

09:30 – 12:30 (with breaks) LECTURES & HANDS-ON COMPUTATIONAL: Single-cell ATACSeq analysis [Alessandro Vitriolo, Cristina Cheroni, Emanuele Villa]

- Pre-processing and QCs: how to evaluate the quality for multiome data?
- Peak calling
- Normalization
- Integration
- Gene Activity

12:30 – 14:00 **LUNCH**

14:00 – 16:00 HANDS-ON COMPUTATIONAL: Single-cell ATACSeq analysis [Alessandro Vitriolo, Emanuele Villa]

- Scoring co-accessibility
- Motif enrichments
- Integration with chromatin capture and derivatives
- Pseudotime and trajectory

16:00 – 16:30 **COFFEE**

16:30 – 18:30 Studying the complexity of brain cells: a glimpse at the benchwork

- Group A: Robotics for multimodal single cell phenotyping in the developing brain [Elena Taverna]
- Group B: Round table and facilities tour «Structuring integrated multi-omic/functional workflows for neural tissue»

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PROGRAMME

DAY 4

Thursday 1 December 2022

	LECTURES: Modelling cell states from single-cell omics data
09.00 – 09.50	(40′ talk + 10′ discussion) [Jose Davila-Velderrain]
09.50 – 10.40	(40′ talk + 10′ discussion) [Shahin Mohammadi]
10:40 – 11:00	**COFFEE**
11.00 – 11.50	(40′ talk + 10′ discussion) [Joshua Welch]
11.50 – 12.40	(40′ talk + 10′ discussion) [Genevieve Lauren Stein-O'Brien]
12:40 – 14:00	**LUNCH**

14:00 – 18:00 (with breaks)	HANDS-ON COMPUTATIONAL: Decomposition-based analysis of single-cell data
	[Jose Davila-Velderrain, Shahin Mohammadi, Asia Zonca]
	• Learning gene expression programs and activity patterns using matrix decomposition
	  ○ ACTIONet
	  ○ CoGAPS
	  ○ Liger
	• Cell clustering vs quantitative transcriptome decomposition
	• Functional interpretation of gene programs
	• Cell type identity vs cell state patterns
	  ○ Dissection of molecular states from brain organoids

18:00 – 21:00	**NETWORKING EVENING**

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PROGRAMME

DAY 5

Friday 2 December 2022

09.30 – 12.30 (with breaks) HANDS-ON COMPUTATIONAL: Multi-omics data integration and network approaches

[Jose Davila-Velderrain, Shahin Mohammadi, Asia Zonca, Daniele Capocefalo]

- Joint transcriptomic and epigenomic analysis (scRNA+scATAC Seq)
    - Alignment-based analysis for independent experiments
    - Multiview learning for same cell multi-omics
- Gene regulatory Network Inference from Single-Cell Data
- Reference data integration: functional interpretation of multi-omic single-cell maps
    - Integrative BrainOmics: PsychENCODE, EpiMap, Roadmap, AllenBrain, GWAS

12:30 – 14:00 **LUNCH**

14:00 – 17:00 (with breaks) COLLABORATIVE PROJECTS ON CASE-STUDIES

Participants will have the opportunity to work collaboratively in small groups applying the analytical techniques learned during the course to case-studies deriving from their own work or from publicly available paradigmatic datasets.

17:00 – 17:30 **CLOSING REMARKS**