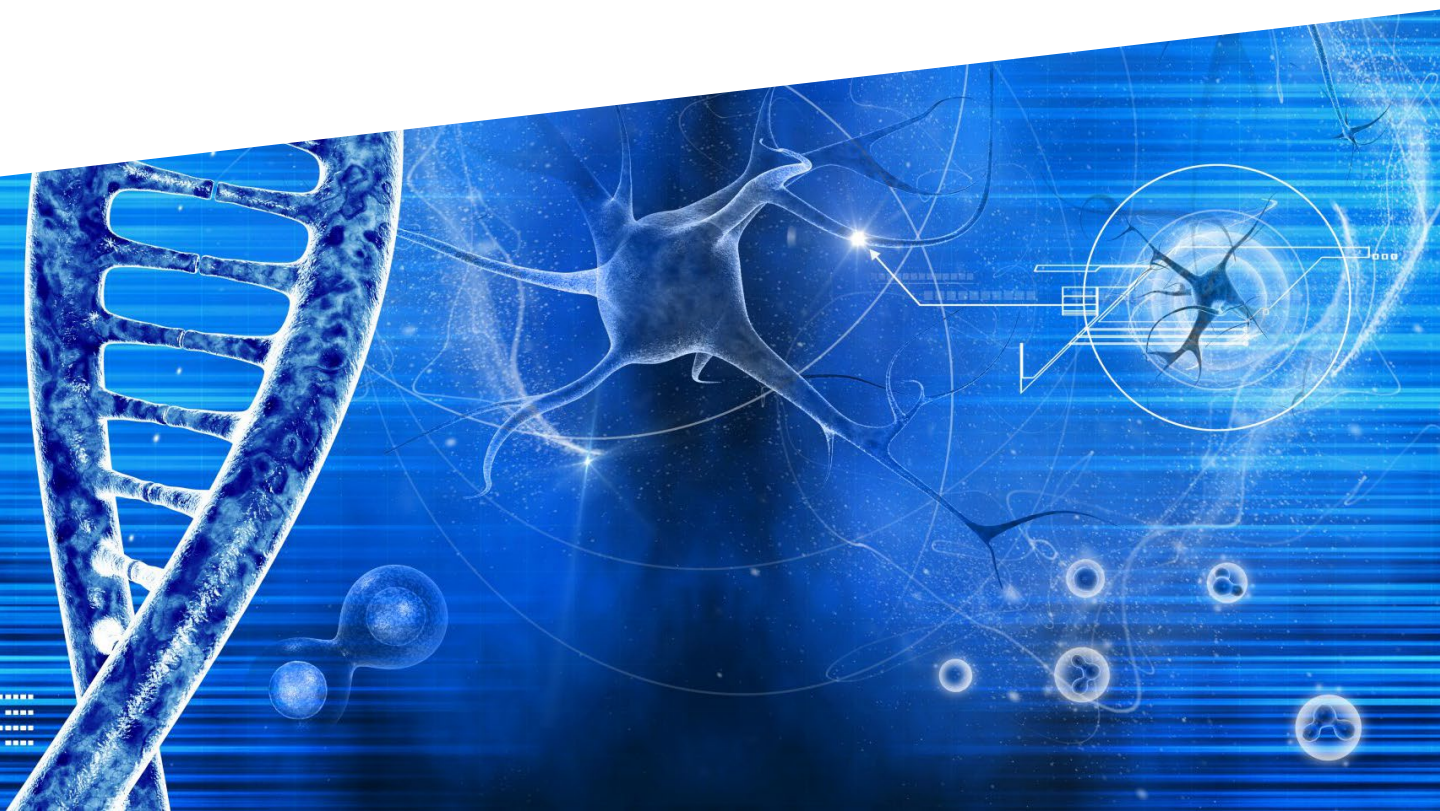


# BRAINOMICS

computational approaches to single-cell  
multi-omics in neuroscience

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



# FACULTY

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## 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 (Altos 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 Capocéfalo (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

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## **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)

# CONCEPT

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## **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.

# PROGRAMME

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DAY 1

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**Monday 28 November 2022**

**09.30 - 10.10** **REGISTRATION & WELCOME COFFEE** / Reception Auditorium

**LECTURES - Chair: Elena Taverna** / Auditorium

**Impact of multi-omics approaches on neurobiology**

**10:10 - 11:00** [Giuseppe Testa] *One by one: organoid-based neurodevelopmental disease modeling at single cell resolution*

**11.00 - 11.50** [J. Gray Camp] *Multimodal spatiotemporal phenotyping of human neural organoids*

**11.50 - 12.40** [Bosiljka Tasic] *Cell types of adult mouse cortex: definition and experimental access*

**12.40 - 14.00** **LUNCH**

**14.00 - 18.00** **HANDS-ON COMPUTATIONAL** / Mezzanine

(with breaks)

**Experimental design and multiplexing 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

**18:00 - 21:30** **NETWORKING EVENING & POSTER SESSION** / HT Restaurant area

(Shuttle leaving from HT at 21:30)

# PROGRAMME

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## DAY 2

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**Tuesday 29 November 2022**

- 09:30 - 10:20** **LECTURES - Chair: Jose Davila-Velderrein / Auditorium**  
**Charting the molecular complexity of brain cells**  
[Peter Kharchenko] *Detecting genetic aberrations in single-cell RNA-seq data*
- 10.20 - 10.50** **COFFEE**
- 10.50 - 11.40** [Gioele La Manno] *Brain development at the single-cell level - heterogeneity and dynamics*
- 11.40 - 12.30** [Elena Taverna] *Choosing to be different: cell biological logic of cell identity and fate choice in the developing brain*
- 12.30 - 14.00** **LUNCH**
- 14.00 - 16.00** **HANDS-ON COMPUTATIONAL / Mezzanine**  
**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** **BREAK**
- 16:30 - 18:45** **Studying the complexity of brain cells: a glimpse at the benchwork / Auditorium & Facilities**  
Round table and facilities tour «Structuring integrated multi-omic/functional workflows for neural tissue»

# PROGRAMME

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DAY 3

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**Wednesday 30 November 2022**

**09:30 - 12:30** **LECTURES & HANDS-ON COMPUTATIONAL** / Mezzanine

(with breaks)

**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** / Mezzanine

**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** **BREAK**

**16:30 - 18:30** **Studying the complexity of brain cells: a**

**glimpse at the benchwork** / Mezzanine & Incubator 3

Robotics for multimodal single cell phenotyping in the developing brain

[Elena Taverna]

# PROGRAMME

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DAY 4

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**Thursday 1 December 2022**

- 09.30 - 10.20** **LECTURES - Chair: Giuseppe Testa / Auditorium**  
**Modelling cell states from single-cell omics data**  
[Jose Davila-Velderrain] *Single-cell analysis of Alzheimer's disease and APOE4-mediated pathogenesis*
- 10.20 - 11.10** [Shahin Mohammadi] *Cell state discovery and annotation in health and disease*
- 11.10 - 11.30** **COFFEE**
- 11.30 - 12.20** [Joshua Welch] *Inferring transcriptome and epigenome dynamics from single-cell multi-omic data*
- 12.20 - 13.10** [Genevieve Lauren Stein-O'Brien] *FROM Cells to circuits: Transfer learning for multimodal data Integration via Latent Spaces*
- 13.10 - 14.00** **LUNCH**
- 14.00 - 18.00** **HANDS-ON COMPUTATIONAL / Mezzanine**  
(with breaks) **Decomposition-based analysis of single-cell data**  
[Jose Davila-Velderrain, Shahin Mohammadi, Asia Zonca]
- Characterizing transcriptional cell states with ACTIONet
  - Network-based cell annotation
  - Horizontal data integration
  - Cell type identity vs cell state patterns
  - Cell clustering vs quantitative transcriptome decomposition
  - Functional interpretation of gene programs
    - Dissection of molecular states from brain organoids
- 20.00 - 22.00** **NETWORKING EVENING / Milan city centre**  
(Shuttle leaving from HT at 19:15)



# PROGRAMME

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## DAY 5

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### Friday 2 December 2022

**09.30 - 12.30** **HANDS-ON COMPUTATIONAL** / Mezzanine

(with breaks)

**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 - 14:50** **CLOSING LECTURE - Chair: Giuseppe Testa** / Auditorium

[Denis Jabaudon]

**14:50 - 18:00** **COLLABORATIVE PROJECTS ON CASE-STUDIES** / Mezzanine

(with breaks)

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.

**18:00 - 18:30** **CLOSING REMARKS**