



Università degli studi dell'Insubria  
Dipartimento di Scienze Teoriche e Applicate



Alta Formazione Insubria

## INTRODUZIONE ALLA SYSTEMS BIOLOGY

*Trascrittomica, proteomica, principi metodologici, analisi statistica*

**29 Giugno - 2 Luglio 2015**

*Docenti: Tiziana Alberio, Mauro Fasano, Riccardo Fesce, Università dell'Insubria;  
Riccardo L. Rossi, Fondazione INGM, Milano.*

**Sede: Università dell'Insubria, Via Alberto da Giussano 12, Busto Arsizio, Aula informatica**

**Orario delle lezioni: 10.00-17.00**

Il corso si propone di introdurre l'analisi statistica di dati "high-throughput" e i metodi per l'interpretazione critica dei risultati attraverso la systems biology.

**Prerequisiti:** Biochimica e biologia molecolare a livello universitario. Conoscenza di base della tecnologia dei microarray e dell'elettroforesi bidimensionale.

**Offerta formativa:** 12 ore teoria + 12 ore pratica

### PROGRAMMA

*Prima giornata - Introduzione alle tecniche post-genomiche (Riccardo Rossi, Tiziana Alberio)*

- ✓ High&medium-throughput data (RTqPCR arrays, DNA microarray)
- ✓ Dati di pubblico dominio: GEO and ArrayExpress
- ✓ Pipeline di analisi dati  
Selezione e identificazione di gene signature; interpretazione funzionale con GSEA; moduli di coespressione e integrazione dati esterni (WGCNA)
- ✓ Next-generation-sequencing  
Cenni sui principali metodi di sequencing; read counts versus average signals; le pipelines di analisi (primaria e secondaria)
- ✓ RNA-seq: confronto con i microarray, vantaggi e differenze.
- ✓ Integrazione e interoperabilità dei dati: verso la Systems Biology
  
- ✓ Studio del proteoma e proteomica differenziale
- ✓ Piattaforme tecnologiche: elettroforesi bidimensionale vs. tecniche gel-free
- ✓ Proteomica differenziale mediante 2-DE e shotgun
- ✓ Principi dell'analisi di immagine. Il database Swiss-2DPage e altre repository di immagini
- ✓ Analisi dei dati proteomici: test parametrici e non parametrici, ANOVA, analisi multivariata
- ✓ Interpretazione dei risultati e costruzione del modello

- ✓ Identificazione sperimentale delle proteine

*Seconda giornata - Statistica per le tecniche post-genomiche (Riccardo Fesce)*

- ✓ test di saggio di ipotesi, parametrici e non (test parametrici e per ranghi, analisi della varianza e equivalenti non parametrici)
- ✓ probabilità composte, indipendenza e correlazione
- ✓ test multipli e relative correzioni
- ✓ concetti e utilità di significatività e likelihood
- ✓ sovrarappresentazione di classi di geni
- ✓ approcci di clustering (Pearson, gerarchie, distanza euclidea)
- ✓ probabilità a priori e a posteriori, teorema di Bayes
- ✓ fattori di rischio, rischio relativo, odds ratios
- ✓ attribuzione di significatività a grafi proteomici e reti di proteine
- ✓ analisi funzionale: sovrarappresentazione di termini di Gene Ontology
- ✓ modelli, test di Fisher, likelihood
- ✓ comparazione di modelli, impiego di modelli ai fini predittivi, analisi ROC

*Terza giornata - Strumenti bioinformatici per la systems biology (I) (Tiziana Alberio, Mauro Fasano)*

- ✓ Reti di proteine, cenni di teoria dei grafi
- ✓ Raggruppamento funzionale delle proteine identificate (GO, KEGG, Reactome)
- ✓ Principi di network enrichment: la necessità di arricchire il modello e gli strumenti web disponibili (String, Bioprofiling, WebGestalt, ...)

*Quarta giornata - Strumenti bioinformatici per la systems biology (II) (Tiziana Alberio, Mauro Fasano)*

- ✓ La piattaforma cytoscape per generare e analizzare reti di geni e proteine
- ✓ App di Cytoscape per trovare sub-networks, per eseguire analisi di sovra-rappresentazione con diversi database di riferimento e per eseguire analisi topologica delle reti
- ✓ Costruzione ed analisi di reti su problematiche sperimentali/metodologiche incontrate dai partecipanti

Ogni sessione prevede parzialmente o totalmente aspetti applicativi attraverso gli strumenti statistici o bioinformatici relativi agli argomenti trattati. Ogni partecipante è invitato a portare dati da analizzare.

## **CV of teachers**

**Mauro Fasano**, Associate Professor of Biochemistry, Department of Theoretical and Applied Sciences, University of Insubria.

Mauro Fasano graduated in Chemistry in 1989 at the University of Torino working on NMR characterization of cell pigments. He later got the Doctorate degree (Chemical sciences, 1992) with a thesis on non-covalent interactions between small paramagnetic molecules and proteins. From 1992 to 2000 he was appointed to the position of Assistant Professor of general chemistry at the University of Torino. Starting from 1st November 2000 he has been appointed as an Associate Professor of Biochemistry at the University of Insubria. He was among the founders of the University outstation in Busto Arsizio establishing there the laboratory of Neuroproteomics and contributing to the development of the Biomedical research division. His research interests are mainly devoted to two main objectives: a) understand molecular mechanisms leading to neurodegeneration to eventually block them by neuroprotective drugs, and b) discover and validate peripheral markers of the disease to allow early and differential diagnosis so that neuroprotective or neurorestorative strategies could be attempted. Both objectives are mainly pursued by means of proteomics techniques, where a first look by a global, hypothesis-free approach is followed by a bioinformatics screening of functional information available in the literature to end up in the generation of a new hypothesis to be confirmed experimentally by classical, hypothesis driven methodologies.

He has been a member of the postgraduate school of molecular and cellular biology of the University of Insubria (2004-2008), and since 2008 he is a member of the Board of Advisors of the postgraduate school of Neurobiology of the University of Insubria. Since 1998 he has been collaborating with the Biotechnology Foundation ([www.fobiotech.org](http://www.fobiotech.org)) in the National School of Bioinformatics. He has been among the founders of the first Master School in Bioinformatics in Italy.

Mauro is an author of about 150 papers on peer-reviewed international journals, as well as on books, edited books, e-books and encyclopedias. He received more than 4000 citations, with h-index = 33 (Source: Elsevier Scopus).

**Tiziana Alberio**, Assistant Professor of Biochemistry, Department of Theoretical and Applied Sciences, University of Insubria.

Tiziana Alberio graduated in Biology Applied to Biomedical Research in 2006 with the thesis "Effects of DeltaNp73beta isoform, overexpressed in a non-small cell lung carcinoma model". She got her Ph.D. in Neurobiology at the University of Insubria in 2010, with the thesis "The proteomic approach to investigate Parkinson's disease: pathogenetic mechanisms and biomarkers discovery". Starting from April 2011, she was the recipient of a postdoctoral research contract from Regione Lombardia (UNIRE). She is currently Assistant Professor of Biochemistry.

Tiziana approached experimental neuroscience during her Ph.D. in Neurobiology, starting from 2007. She developed cellular models to investigate the processes at the basis of Parkinson's disease and to test the possibility to use lymphocytes as a source for peripheral biomarker of the disease. In both cases, she used a proteomic approach. During the two-year post-doc, she developed a panel of lymphocyte biomarkers, as a model to discriminate Parkinson's disease patients. She was listed as inventor in an international patent on this panel. She participated in an industrial collaborative project on the proteomic analysis of plasma from Parkinson's disease patients and she deepened her knowledge about protein networks to interpret proteomic results.

Tiziana acted as peer-reviewer for several scientific journals in the field, including *Frontiers in Genetics*, *EuPA Open Proteomics* and *Journal of Proteomics*. She is author of 20 publications on peer-reviewed international journals.

**Riccardo Fesce**, MD, Full Professor of Physiology, Department of Theoretical and Applied Sciences, University of Insubria.

Riccardo Fesce graduated in Medicine in 1979 at the University of Milano working on the ultrastructural alterations in the presynaptic membrane that accompany quantal release of acetylcholine at the neuromuscular junction. He later got his Specialisation Diploma in Medical Pharmacology (1985) with a thesis on the pharmacokinetics of closed circuit anaesthesia. From 1983 to 1985 he worked as a Research Associate at the Biophysics Department of the Rockefeller University, New York, NY, and developed a novel

approach for measuring quantal release of neurotransmitters by means of a modification of noise analysis procedures. His expertise in statistical and stochastic approaches to signal analysis was recognized by an invited review in *Progress in Neurobiology: "Stochastic Approaches to the Study of Synaptic Transmission"*. From 1985 to 2001 he was Research Associate at the National Research Council (CNR) Centre of Cytopharmacology in Milano. He mostly worked on the establishment of the vesicle hypothesis of quantal secretion, using and correlating morphological (EM, freeze fracture, quick freezing) and electrophysiological data. He also studied synaptic transmission and sensory signal processing at the cytoneural junction of the labyrinthine posterior canal. In 2001 he was appointed Associated Professor and in 2006 Full Professor (Physiology) at Insubria University. In addition to continuing his studies on synaptic transmission and signal processing, he developed a set of primers for RNA fingerprinting by in silico simulation and developed a molecular model for the GABA Na-Cl-dependent neurotransporter.

He was among the founders of the Research Centre for Neuroscience at Insubria University (2003). He also was among the founders of the postgraduate school of Neurobiology at the same University (2005), and has been a member of the Board of Advisors ever since.

Since 1990 he has led a number of research projects, funded by CNR or the Italian Ministry for Research (Strategical Projects, National Interest Projects), on the physio-pharmacology of synaptic function at labyrinthine organs, on synaptic transmission at the sympathetic ganglia, and on the development of biotechnological methods (concomitant electrophysiological and calcium imaging measurements) in neuronal cell cultures.

He is an author of more of 60 papers in peer-reviewed international journals, in addition to contributions to books and encyclopedias.

**Riccardo Lorenzo Rossi**, PhD. Head of Computational Biology and Data Analysis, Fondazione Istituto Nazionale di Genetica Molecolare (INGM), Milano.

Riccardo L. Rossi graduated in biological sciences at the University of Milan with a thesis on budding yeast cell cycle, working on glucose mediated cell cycle regulation. He then obtained his PhD in Industrial Biotechnology at the University of Milano-Bicocca with a thesis on innovative flow cytometry-based multiparametric detection methods applied to budding yeast research and then working on systems biology approaches to cell cycle regulation. During a two year post doc period spent at the Department of Biochemistry of the University of Washington in Seattle, USA, he deepened his knowledge on metabolic transcriptional regulation of budding yeast.

Back in Italy in 2008, Riccardo moved to INGM where he approached molecular immunology, working on microRNA mediated regulatory transcriptional networks in human lymphocytes. He specialized in microRNA research, medium and high throughput gene and microRNA expression; he authored papers and an international patent on microRNAs as regulators and biomarkers. He currently coordinates a group of computational biologists and informaticians working on high throughput data - mainly transcriptomics, arrays and ngs - generated in the Institute; he and his colleagues are involved in an effort of introducing computational techniques in the realm of biological and clinical data trying to efficiently integrate them.

## Sede del Corso:

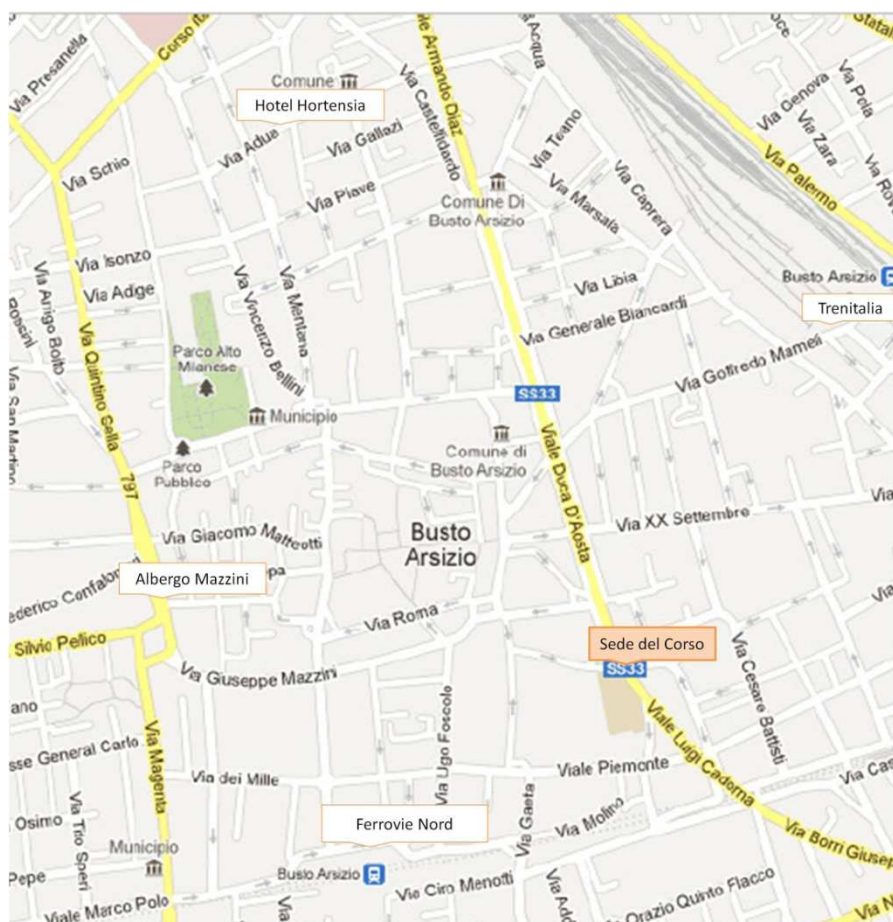
Aula informatica Università dell'Insubria, Via Alberto da Giussano, 12, 21052 Busto Arsizio

## Come arrivare:

**In treno:** Raggiungere le stazioni di Busto Arsizio (via Milano Porta Garibaldi o Passante Ferroviario) o Busto Arsizio Nord (via Novara, Milano Cadorna, Milano Bovisa, Milano Centrale o Milano Porta Garibaldi). Orari consultabili su <http://www.fsitaliane.it/>. Seguire le indicazioni della mappa.

**In Auto:** Uscire a Busto Arsizio (A8) o Marcallo Mesero (A4, poi superstrada per Malpensa e uscita Vanzaghello) e raggiungere il parcheggio di Piazzale dei Bersaglieri (non disponibile il giovedì). Coordinate GPS 45.607621, 8.857178.

**In Aereo:** Per chi vola a Milano Linate è consigliabile raggiungere Milano Centrale e seguire le indicazioni per chi viaggia in treno. Percorrenza 65 minuti circa. È consigliabile volare su Milano Malpensa e prendere il Malpensa Express (dal Terminal 1 - orari consultabili su [www.trenord.it/](http://www.trenord.it/)) scendendo a Busto Arsizio Nord. Percorrenza 9 minuti.



## Indicazioni per il pernottamento:

### A 10-15 minuti a piedi:

Hotel Ortensia (\*\*\*) <http://www.hotelhortensia.it/>

Albergo Mazzini (\*\*\*) <http://www.albergomazzini.it/>

### Raggiungibili solo con mezzo proprio:

Hotel Pineta (\*\*\*\*) <http://pineta.lerobinie.com/>

Hotel Le Robinie (\*\*\*\*) <http://www.lerobinie.com/>

È disponibile un servizio di prenotazione alberghiera tramite Varese Convention & Visitors Bureau ([congressi@vareseturismo.it](mailto:congressi@vareseturismo.it)).

## Modalità di partecipazione

Il corso è a numero chiuso, con 20 posti disponibili che vengono assegnati in ordine di iscrizione. Il corso sarà attivato solo al raggiungimento minimo di 10 iscrizioni. Le date di erogazione del corso potranno subire modifiche legate ad esigenze dell'organizzazione.

## Quote individuali di iscrizione:

<u>Entro 29 maggio 2015</u> € 440.00 + IVA*	<u>Dopo 29 maggio 2015</u> € 540.00 + IVA*
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\*In caso di esenzione IVA, allegare documentazione.

Informazioni, [CONDIZIONI GENERALI](#) e modulo di iscrizione: [www.afinsubria.org](http://www.afinsubria.org)

Pagamento da effettuare con bonifico bancario **dopo la conferma dell'attivazione del corso** da parte della Segreteria Organizzativa:

IBAN IT23X0558450233000000000229

BIC/SWIFT BPMIITMMXXX CIN X

**Causale: Nome Cognome corso Systems biology 2015**

### Segreteria scientifica e organizzativa:

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## Con il Patrocinio di

