1st qBio mini-Workshop

Short scientific profiles of participating groups

In alphabetic order – speaker's last name

Beatrice Bodega, *Speaker*

Genome Biology Unit - INGM

The epigenetics field is finally approaching the function of non-coding repetitive genome. The work of Genome Biology team may provide important mechanistic information and novel interpretation of how specific non coding DNA functions may directly influence cellular processes, such as differentiation and disease. Ultimate goal that to demonstrate that evolutionary acquisition of such elaborated fine modulation of transcription represent an added value for mammalians, and humans in particular, to react to environment, adapt to stress, and eventually predispose to better or worse outcomes in disease progression. Such an effort in elucidating DNA repeats molecular mechanisms might at the end get genome biology and epigenetics research closer to truly effective forms of personalized medicine.

Stefano Campaner, *Speaker*

Cancer Biology Unit - IIT

Cancer represents a collection of pathologies characterized by the selective accumulation of alterations in the genome (point mutations, rearrangements, amplifications, deletions) and the epigenome (DNA methylation and histone modifications) leading to aberrant cell growth. The main focus of our research is the characterization of key transcription factors (Myc and YAP/TAZ) that are aberrantly activated in cancer with the primary goals of (i) understanding how they induce cell transformation and (ii) identifying specific cancer cells vulnerabilities. This entails the genetic and epigenetic analysis of tumor progression, using conditional mouse models and the use of reverse genetics approaches based on either viral ShRNA (for in-vivo screens) or siRNA based high-content screens.

Alessandra Carbone, Elodie Laine, Hugues Richard, *Speakers*

Analytical Genomics - CQB, Alessandra Carbone

The group works on various problems connected with the functioning and evolution of biological systems. Mathematical methods coming from statistics and combinatorics, as well as algorithmic tools are employed to study fundamental principles of the cellular functioning starting from genomic data. The projects developed by the group are all aimed at understanding the basic principles of evolution and co-evolution of molecular structures in the cell. They concern the sequence evolution of entire genomes as well as protein evolution. A. Carbone is the director of the Department of Computational and Quantitative Biology, created in January 2009 by CNRS and UPMC with the aim of developing an interdisciplinary working environment made of several groups of theoreticians and experimentalists interested in bioinformatics and modeling of complex biological systems, systems biology, population genetics. A. Carbone received the Prix Joliot-Curie in 2010 from the French Ministry of Research and the EADS Foundation, and in 2012 the Grammaticakis-Neuman Prize of the French Academy of Science for "Integrative Biology". From 2013 she is a senior member of the Institut Universitaire de France.

Stefano Casola, *Speaker*

Genetics of B cells and lymphomas unit - IFOM

Stefano Casola is a molecular oncologist specialized in studying the mechanisms controlling B lymphocyte differentiation and malignant B cell transformation. Applying genome-editing tools to pre-clinical mouse and human models, together with genomic and epigenomic analyses on human lymphomas, the Casola group is interested to identify the major genetic and epigenetic determinants controlling germinal center B cell physiology and malignant B cell transformation. The ultimate goal is to apply this knowledge to improve current treatments of malignant B cell neoplasia.

Yuting Chen, *Speaker*

Genetic code reprograming and synthetic biology - CQB UPMC, Shixin Ye–Lemann

The Ye–Lemann group works on applying genomic editing tools in mice and rats, such as CRISPR/Cas system, TALENs, and transposon systems. Since 2014, they lead a collaborative project to expand the genetic code in mice and zebrafish. They demonstrated the feasibility in mice inheriting the orthogonal aminoacyl-tRNA synthetase and suppressor tRNA gene, which recodes the amber codon to the unnatural amino acid, the p-azido-L-phenylalanine. This results have been recently published in Cell Research and highlighted in Science.

Matteo Cristofalo, *Speaker*

Biophysics and Biomedical physics - UNIMIB, Francesco Mantegazza

Coming from a background in the fields of Optics, Complex Fluids and Soft Matter, our group is focused on single molecule experiments both on DNA and proteins. Overall, in the study of the biopolymers structure and function by a single molecule approach, the molecule itself could be the real object of study and its proprieties could be monitored as concrete values, not as an averaging from millions of molecules. In particular, we are interested in the nanomechanical properties of DNA: from the study of bare DNA to more complex systems such as DNA superstructures (G quadruplexes, Holliday junctions…), DNA/protein complexes (H-NS, Fis protein…), and the DNA interactions with anticancer drugs, by means of Magnetic Tweezers (MT) and Atomic Force Microscopy (AFM).In addition, by using AFM in Force Spectroscopy mode, we study the nanomechanical kinetics of the unfolding and refolding pathways of single protein. Furthermore, we investigate the surface elasticity of cell membranes and extracellular matrix in order to correlate its properties with the cells behavior.
We also perform *in vivo* calcium imaging and we study single cell signaling in fluorescence by means of confocal spinning disk microscopy.
Finally, we contribute to the Nanomedicine field by characterizing nanoparticles for drug delivery and amyloid aggregation kinetic (fibrils and oligomers) and its regulation nanoparticles-mediated by means of AFM as well as of advanced fluorescence techniques.

Andrea Ciliberto, *Speaker*

Quantitative Biology of Cell Division - IFOM

Chromosome segregation requires the proper separation of sister chromatids between daughter cells. This process is doubly relevant for studying cancer. On the one hand, if segregation is not accurate, cells may become aneuploid, a typical feature of cancer cells. On the other hand, the pathway that supervises chromsome segregation is invoked by many anti-mitotic drugs to arrest cell proliferation. Our group is interested to understanding the principles that regulate chromosome segregation, especially in a context where the process is impaired. Such conditions somehow mimics what happens in cells treated with by anti-mititotic drugs. To address these issues, our lab uses a combination of mathematical models and typical tools of quantitative biology, especially single cell imaging.

Ylli Doksani, *Speaker*

Replication Stress Response - IFOM

Ylli Doksani did his PhD in Marco Foiani's lab where he studied the mechanisms that deal with double strand breaks during DNA replication. As a post doc he moved in Titia de Lange's lab at the Rockefeller University in New York, where he studied telomere end protection showing that the shelterin component TRF2 is required for the formation of t-loop structures at telomeres. Since April 2016 is a group leader in IFOM where he studies the mechanisms of replication stress response at telomeres.

Chiara Enrico-Bena, *Speaker*

Quantitative biology group - Hugef and PoliTO, Carla Bosia

Our project is inspired by a quantitative approach recently developed in microbiology and mainly concerns mammalian cell physiology. It is focused on the identification of a link between cancer cell physiology, cell growth and the strategy of internal partitioning of resources inside the cells. With a constant interplay between mathematical modelling and wet-lab experiments, we point toward a phenomenological large-scale description of cell physiology able to be predictive even in absence of a complete knowledge of molecular details. We also study mechanisms and consequences of the interaction between microRNAs (miRNAs) and their target messenger RNAs (mRNAs).

Christoph Feinauer, *Speaker*

Statistical Genomics and Biological Physics - CQB-UPMC, Martin Weigt

Biology is becoming a data rich science. Based on a background in statistical physics and machine learning, the "Statistical Genomics and Biological Physics" team develops algorithmic approaches for extracting biological information, which is hidden in large-scale data sets. The central example for our work is the coevolutionary analysis (the so-called direct-coupling analysis) of the sequence variability of homologous proteins across thousands of species, to unveil the three-dimensional protein structure, interactions between proteins, and the fitness effect of mutations.

Francesco Ferrari, *Speaker*

Computational Genomics - IFOM

Francesco Ferrari obtained his PhD in Biotechnology and Molecular Medicine in 2008 from the University of Modena and Reggio Emilia. He then specialized in computational biology and genomics. After a first postdoc at the University of Padova, he joined the group of Peter J. Park at Harvard Medical School where he worked on the use of high-throughput sequencing techniques to study chromatin and transcription dynamics in different experimental models. In 2015 he joined IFOM as group leader of the "Computational Genomics Laboratory". His laboratory is particularly focused on understanding the role of chromatin organization and epigenetics in regulating gene expression, and how these mechanisms are altered in cancer.

Gilles Fischer, *Speaker*

Biology of Genomes - CQB-UPMC

The Biology of Genomes team (http://www.lcqb.upmc.fr/BIG) in the Laboratory of Computational and Quantitative Biology develops both experimental and computational approaches to understand the mechanisms of genome evolution in yeast. The main research foci in the team include the reconstruction of ancestral genomes, the role of DNA replication in genome evolution, the emergence of new genes, the formation of chromosomal rearrangements and the evolution of the replication program. Gilles Fischer started his career working on the physical mapping and the structural instability of the linear chromosome in an Actinomycetes bacteria called Streptomyces. He obtained a PhD in Genetics from the University of Nancy (France) and moved to the University of Oxford (UK) as a post-doctoral fellow where he started working on yeast genome evolution. He was then recruited at the CNRS and joined the Institut Pasteur in Paris where he pursued experimental work to decipher the mechanisms of formation of large segmental duplications and started comparative genomics studies, as a member of the Génolevures program.

Marco Foiani, Gururaj Kidiyoor, *Speakers*

Genome Integrity - IFOM, Marco Foiani

The research interest of this team focuses on the regulatory mechanisms that control genome integrity. Prof. Marco Foiani is the Scientific Director and Head of the Genome Integrity Laboratory of IFOM - The FIRC Institute of Molecular Oncology Foundation and co-founder of the IFOM-IEO Campus. He was the founder and Vice-President of the European Nanomedicine Foundation (CEN). He is member of the Scientific Advisory Board of AIRC and Full Professor in Molecular Biology at the University of Milan and Professor at the European School of Molecular Medicine (SEMM). He is member of the editorial board of Cell and EMBO member

Marco Gherardi, Matteo Osella, *Speakers*

Genomic Physics - CQB UPMC / IFOM, Marco Cosentino Lagomarsino

Our group combines tools from theoretical physics (statistical mechanics, soft condensed matter, hydrodynamics), to study biological questions concerning genomes and the cells that carry them. We favor a bottom-up approach where simple models are gradually constructed from data analysis and experiments. Our current main topics are single-cell physiology (growth and cell-cycle control), chromosome organization, and, in evolutionary genomics, the laws that determine the partitioning of genomes into functional and evolutionary elements.

Francesco Ghini, *Speaker*

Center for genomic Science - IIT, Francesco Nicassio

The recent discovery of thousands of non-coding RNAs (ncRNAs) with regulatory function is redefining the landscape of transcriptome regulation, highlighting the interplay of epigenetic, transcriptional and post-transcriptional mechanisms. We have witnessed to the identification of an increasing number of either small regulatory RNAs (such as microRNAs, miRNAs) or long non-coding RNAs (lncRNAs). However, the definition of their upstream regulatory pathways or downstream molecular functions are still open questions, under intense investigation worldwide. Our general aim is to provide a critical and original contribution towards the understanding of the role played by non-coding RNAs in shaping the cell transcriptome, both in physiology and cancer.We are pursuing this goal by investigating qualitatively and qualitatively the modes and the mechanisms of action of non-coding RNAs within specific biological contexts, exploiting a combination of high-throughput genomic approaches, *in silico* analysis and sophisticated experimental models. Current research lines are centered on:

- the characterization of microRNAs and long non-coding RNAs in control of the 'stemness' transcriptional program in normal and tumor tissues of the breast
- microRNA degradation mechanisms and interplay with RNA targets: the Target-induced miRNA degradation (TIMD)

Fabio Iannelli, *Speaker*

DNA Damage Response and Cellular Senescence - IFOM, Fabrizio d'Adda di Fagagna

Fabio Iannelli is a senior postdoc in the group of Fabrizio d'Adda di Fagagna (FdAdF) where he is currently studying the events shaping gene expression after the induction of DNA damage. FdAdF group studies the DNA damage response (DDR), a signaling and effector pathway that coordinates cell-cycle arrest and DNA repair. We recently discovered that RNA modulates DDR activities, including signaling and checkpoint functions, unveiling a novel layer of DDR regulation dictated by RNA molecules. We have also developed new tools to detect in situ DSBs and a new target enrichment method to detect novel small RNA species, and we are applying these approaches to ongoing studies ranging from *in vitro* cell systems to neurodegenerative disorders

Daniel Jost, *Speaker*

TIMC-IMAG Lab - University Grenoble-Alpes - CNRS

Accessibility of transcription factors to promoter is controlled by biochemical modifications of DNA or histone tails which modulate gene expression without alteration of the genetic information. Propagation, maintenance and inheritance of these epigenetic marks are crucial mechanisms in development, phenotype stabilization and disease.
In close collaboration with biologists, we develop quantitative models (based on polymer and statistical physics) of various aspects of epigenetic mechanisms at multiple scales. In particular, we are focusing on the stochastic properties of epigenetic markers at the gene level and on the dynamic coupling between 3D chromatin organization and epigenome at the chromosome scale. Applications of our models go from the deregulation of epigenetic memory in cancer to the formation of topologically-associated domains in drosophila and mammals or to the dosage compensation in worms.

Chiara Lanzuolo, *Speaker*

Chromatin and Nuclear architecture Laboratory - IBCN-CNR

The group is devoted to understanding how the genome folding occurs in the nuclear space finding the right orientation and nuclear position and how this conformation is then maintained or regulated in dynamic physiological processes in health and in disease. Chiara Lanzuolo obtained a degree with honours in Biological Sciences, at University of Naples "Federico II" in 1998, and, in 2002, she obtained her PhD in Genetics at the Ecole Normale Superieure of Lyon, France. From 2002 to 2009, she worked as "postdoctoral research scientist" in Dulbecco Telethon Institute, at the Institute of Genetics and Biophysics (IGB-CNR) Naples, Italy and then at the Institute of Cellular Biology and Neurobiology (IBCN-CNR) Rome, Italy. From 2009 Chiara Lanzuolo holds a three years Researcher position at Institute of Cellular Biology and Neurobiology (IBCN-CNR) Rome, Italy. In 2011 Dr. Lanzuolo was awarded by MIUR (Italian Ministry of Research and University), with the grant "Futuro in ricerca 2010" to start her independent research activity.

Paolo Maiuri, *Speaker*

Spatiotemporal organization of the nucleus - IFOM

Paolo Maiuri is a biophysicist with experience in quantitative biology. He conducted studies in different fields of research, from HIV transcription to single cell migration. The main interest of his recently established laboratory is to investigate the interplay between cell architecture and nuclear organization. The spatiotemporal organization of the genome in the nucleus of eukaryotic cells is dynamic and contributes to the regulation of gene expression, but how does it respond to the changes of cell morphology is an unexplored area of research. We wish therefore to study if and how physical cues that affect cell morphology could also influence the three-dimensional organization of the nucleus leading to
changes of gene expression patterns. Understanding cell morphology-induced changes of nuclear chromatin is of importance not only to understand the fundamental relationship between cell geometry and gene expression but also to elucidate its possible implication in diseases.

Thierry Mora, *Speaker*

Laboratoire de physique statistique - ENS

My research interests lie in the statistical modeling of complex biological systems with many correlated units, from proteins to group behaviour, based on high-throughput biological data, and spanning different biological fields including neuroscience, biophysics and immunology. In neuroscience, I study how populations of neurons collectively encode visual information in the retina. In animal behaviour, I study how local interactions between individuals lead to overall coordination of the group. In immunology, I develop statistical methods to understand immune repertoire diversity from sequence data, and use mathematical tools to study repertoire dynamics and function.

Marco Morelli, *Speaker*

Oncogenes, chromatin and cell cycle control - IIT, Bruno Amati

Marco Morelli is a researcher at the Center for Genomic Science of the Italian Institute of Technology in Milan. After a M.Sc. in theoretical physics at the University of Pavia (Italy), he moved to the AMOLF institute in Amsterdam for a PhD in Biophysics under the supervision of Prof. Daan Frenkel and Prof. Pieter Rein ten Wolde, where he studied the impact of spatial and temporal fluctuations on regulatory networks in bacteria. He moved to the University of Glasgow for a postdoc in the group of Prof. Dan Haydon, where he investigated the genetic structure of a viral quasispecies during a chain of infection and he developed a model to infer the most probable route of infection during an epidemic outbreak using both epidemiological and genetic data. Since 2012 he moved in his current position where he coordinates the computational activities of the Bruno Amati's group, focusing on the development of new methods to analyze epigenomic data and on the characterization of Myc-driven lymphomas.

Vittore Scolari, *Speaker*

Spatial regulation of genomes - Institut Pasteur, Romain Koszul

Our research is focusing on the interplay between chromosome dynamics, cell cycle, and consequences on chromosome stability, that we study principally on microorganisms.
To do so, we use a combination of genome-wide and single-cell technologies (3C, Hi-C, imaging), synthetic methods (neo-chromosome assembly), as well as *in silico* and *in vivo* approaches.
We also develop computational techniques aiming at improving genome assembly and metagenomic/pan-genomic analysis through the exploitation of chromosome physical D signatures.
Vittore Scolari is a postdoc in our group, his research is on the analysis and physical modeling of 3C datasets, particularly focusing on the dynamics of Yeast chromosomes under experimental conditions and along the cell cycle.

Guido Tiana, *Speaker*

Theoretical Biophysics Lab, UNIMI

In the Laboratory of Theoretical Biophysics at the University of Milano we study the physics of complex systems, mainly of biological interest, with the help of the methods coming from statistical mechanics, making also heavy use of computational tools. In this way, we have investigated protein folding, aggregation, molecular evolution, drug design, genetic networks and, recently, the conformational properties of chromosomes. In a nutshell, we study models, that is simplified descriptions of complex systems, strongly rooted into experimental quantitative data. The goal is that of finding the simplest rules that control the complex phenomena that take place in the cell, and eventually to be predictive about them.

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CQB, Computational and Quantitative Biology. UMR7238 CNRS, Sorbonne Universités, Université Pierre et Marie Curie Paris, France

ENS, École normale supérieure, Paris, France

HuGeF, Human Genetics Foundation, Politecnico di Torino, Italy

IIT, Istituto Italiano di Tecnologia, Italy

IFOM, the FIRC Institute of Molecular Oncology, Milan, Italy

INGM, Istituto Nazionale di Genetica Molecolare, Milan, Italy

UNIMIB University of Milano-Bicocca, Italy

UNIMI, Università degli Studi di Milano, Italy

Institute of Cell Biology and Neurobiology (IBCN) - CNR