DSV Seminars

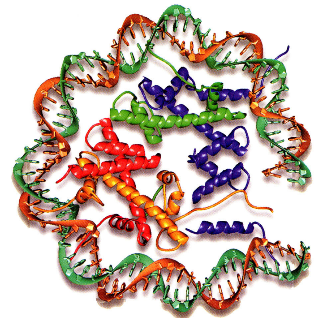
UNIVERSITÀ DEGLI STUDI DI TRIESTE

DIPARTIMENTO DI SCIENZE DELLA VITA

PhD Program in Molecular Biomedicine and JUMBO PhD

November 24, 2017 - 11:00

Seminar Room, Building Q – Via Giorgieri, 5 Trieste



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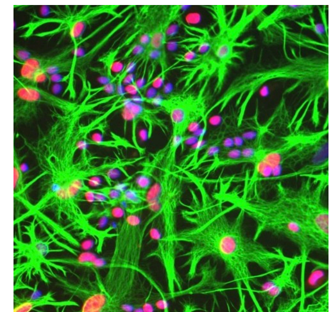
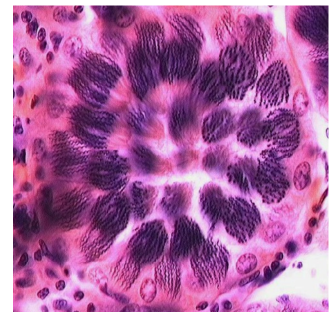


Computational methods to explore chromatin architecture



The 3D organization of chromatin within the nucleus is crucial for genome functionality. This is true at multiple levels: on a large scale, with chromosomes occupying distinct volumes (territories), at the level of individual chromatin fibers, organized in compartmentalized domains (as the Topologically Associating Domains, TADs), and down to the short range chromatin interactions. The widespread adoption of high-throughput techniques derived from Chromosome Conformation Capture (3C) has been instrumental in the knowledge of chromatin nuclear organization. In particular, Hi-C has the potential to achieve the most comprehensive characterization of chromatin 3D interactions, as it allows detecting any pair of fragments connected as a result of ligation by proximity. The analysis of the enormous amount of data produced by Hi-C required the development of *ad hoc* algorithms and procedures. Despite the increasing number of pipelines, no consensus on the optimal approach has been reached yet. Here we will present a quantitative comparison of the performances of Hi-C data analysis methods for the identification of multi-scale chromatin structures using experimental and simulated data. We will also address tool usability including running time and computational requirements. We will show that, depending on the tool, identified structures vary in terms of quantity and characteristics and are more reproducible for TADs than for interactions. Moreover, we will demonstrate how the various tools greatly differ in terms of usability, interoperability, stability of the implementation, and computing resources required to complete the analysis. Results from this comparison evidenced some crucial limitations of TAD callers, the inefficacy in capturing subtle interaction patterns within the domains and changes in the chromatin architecture. We will thus present how we addressed these limitations through TAD-AH (TADs Advanced Hierarchy), a computational procedure for the characterization of both static and dynamically changing chromatin domains.