SEMINAR

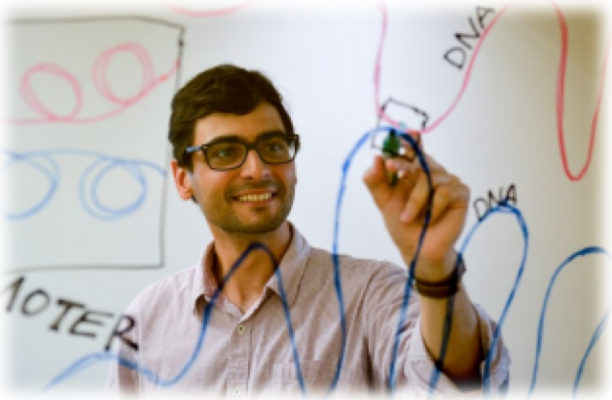
contact: zach.hensel@itqb.unl.pt (please contact if you want to meet the speaker)

INSTITUTO DE TECNOLOGIA QUÍMICA E BIOLÓGICA ANTÓNIO XAVIER | WWW.ITQB.UNL.PT

Comparing mitotic and interphase chromosome conformation at single-cell resolution

Monday April 23, 11:00–12:00

ITQB Auditorium



Dr. Filipe Tavares-Cadete

Abstract

The conformation of the DNA inside the nucleus has been studied using a variety of Chromosome Conformation Capture (3C) techniques, from the original 3C to genome-wide Hi-C variants. The readout of these techniques consists of DNA-DNA pairwise interactions that occur in a population of cells. However, such population-based interaction maps do not reveal which interactions co-occur in single cells. Current single-cell Hi-C methods have poor spatial resolution and the number of interactions captured per cell is relatively low so that co-occurring interactions at specific loci or local higher order 3D structures are rarely captured. A new variation on 3C called CWalk can detect non-pairwise interactions in single cells, taking advantage of the fact that 3C constructs include several fragments that are in close spatial proximity. These CWalks provide unique information about groups of co-occurring pair-wise interactions that represent local higher order 3D chromosome structures. We have combined the 3C protocol with long-read sequencing to detect groups of interactions that occur in the same cell and developed a data processing pipeline specific for this data. We have applied this method to analyze chromosome conformation in interphase and mitotic HeLa S3 cells. Our data reveal different patterns of co-occurring interactions in interphase and mitosis. Comparison with Cwalks simulated from pair-wise Hi-C experiments confirm cell cycle stage specific formation of compartments and TADs and shows that real walks are more constrained in their genomic span. In mitosis this constraint appears around 10Mbp, the distance between predicted layers of loops that define the folding of mitotic chromosomes as we previously proposed. Co-occurring interactions reveal interdependencies that cannot be predicted from Hi-C data and these reflect higher order chromosome structures such as interfaces between TADs, between compartments and between chromosomes as they occur in single cells.