Contribution ID : **33** Type : **Oral**

Multiscale modelling of chromatin 4D organization in SARS-CoV-2 infected cells

SARS-CoV-2 is able to re-structure chromatin organization and alters the epigenomic landscape of the host genome, though the mechanisms that produce such changes are still poorly understood. Here, we investigate with polymer physics chromatin reorganization of the host genome, in space and time upon SARS-CoV-2 viral infection. We show that re-structuring of A/B compartments is well explained by a remodulation of intra-compartment homotypic affinities, which leads to the weakening of A-A interactions and enhances A-B mixing. At TAD level, re-arrangements are physically described by a general reduction of the loop extrusion activity coupled with an alteration of chromatin phase-separation properties, resulting in more intermingling between different TADs and spread in space of TADs themselves. In addition, the architecture of loci relevant to the antiviral interferon (IFN) response, such as DDX58 or IFIT, results more variable within the 3D single-molecule population of the infected model, suggesting that viral infection leads to a loss of chromatin structural specificity. Analysis of time trajectories of pairwise gene-enhancer and higher-order contacts reveals that such variability derives from a more fluctuating dynamics in infected case, suggesting that SARS-CoV-2 alters gene regulation by impacting the stability of the contact network in time. Overall, our study provides the first polymer-physics based 4D reconstruction of SARS-CoV-2 infected genome with mechanistic insights on the consequent gene misregulation.

Primary author(s) : Dr. CHIARIELLO, Andrea Maria (Dipartimento di Fisica Ettore Pancini, Università di Napoli Federico II)

Presenter(s) : Dr. CHIARIELLO, Andrea Maria (Dipartimento di Fisica Ettore Pancini, Università di Napoli Federico II)

Session Classification : Physics of Life

Track Classification : Physics of life