

Polymer physics models predict 3D chromatin organization of SARS-CoV-2 infected cells

It has been recently discovered that SARS-CoV-2 alters chromatin 3D structure of the host genome [1] at multiple length scales, ranging from some kbp to entire chromosomes. We use polymer-physics models to investigate the physical mechanisms underlying such re-structuring. In particular, we show that a polymer model with altered chromatin phase-separation properties [3] accurately captures re-arrangements upon viral infection, as emerged from experimental data. Furthermore, Molecular Dynamics (MD) simulations of the model indicate that SARS-CoV-2 infection leads to a peculiar loss of structural specificity and impacts chromatin time dynamics, reducing the stability of the regulatory contact network of key genes involved in the antiviral response. Overall, this study [3] provides the first polymer-physics based 4D reconstruction of SARS-CoV-2 infected genome with mechanistic insights on the consequent gene mis-regulation.

[1] R. Wang, *et al.*, SARS-CoV-2 restructures host chromatin architecture. *Nat. Microbiol.* **8**, 679-694 (2023).

[2] A. M. Chiariello, *et al.*, Polymer physics of chromosome large-scale 3D organisation. *Sci. Rep.* **6**, 29775 (2016).

[3] A. M. Chiariello, A. Abraham, S. Bianco, A. Esposito, A. Fontana, F. Vercellone, M. Conte, M. Nicodemi, Multiscale modelling of chromatin 4D organization in SARS-CoV-2 infected cells. *Nat. Comm.* **15**, 1-13 (2024).

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