Tracking the nuclear wide dynamics of live cell nucleosome proximity by fluorescence anisotropy imaging of histone FRET

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Inside the nucleus of an intact cell, DNA is folded around histone proteins into nucleosomes and compacted into a multi-layered three-dimensional chromatin network. The nanometer spacing between nucleosomes positioned throughout this structural framework is known to locally modulate local DNA template access and regulate genome function [1]. However, given that this structural feature occurs on a spatial scale well below the diffraction limit of optical microscopy, real time observation of nucleosome proximity in live cells has proven technically difficult, despite recent advances in live cell super resolution imaging [2]. Here we present a powerful and new alternative solution that is based on fluorescence anisotropy imaging microscopy (FAIM) of Förster resonance energy transfer (FRET) between fluorescently labelled histones – the core protein of a nucleosome. FAIM of histone FRET enables a super-resolved readout of nucleosome proximity throughout the nuclear landscape of a living cell to be monitored with millisecond temporal resolution. From application of this technology to the study of global chromatin network dynamics, we find nucleosome proximity to temporally oscillate between different spacings when chromatin is in an open compaction state. We propose that this plasticity in nucleosome positioning is important for spatiotemporal regulation of transcription.

[1] Lou, J.... E. Hinde (2019). PNAS 116 (15).
[2] Lou, J.... E. Hinde (2021). Front. Genet. 12 (770081).