IN SITU SEQUENCING: TOWARDS A HOLISTIC VIEW OF GENOME ARCHITECTURE DURING INTERPHASE

Understanding the 3D arrangement of the 46 DNA molecules during interphase has been, and still is, a real challenge due to limitations of the available tools.
The use of Multicolor FISH and confocal microscopy led to the discovery of chromosome territories and large scale organization of DNA but the resolution was limited by optical constraints. Chromosome conformation capture technology, based on crosslinking of adjacent DNA sequences has been associated with massively parallel sequencing in Hi-C technique and allows one to understand the arrangement at the DNA loop level where interactions occur. However, this tool only gives an average view from the multiple cells used, which may be different from one cell to another.
Realizing that most modern sequencers are a kind of "microscope" reading a fluorescent signal emitted after each round of nucleotide incorporation, several teams started working on *in situ* sequencing, in order to obtain images of the chromosome conformation by imaging the position of the sequenced tags. Furthermore, these technologies can also image other nuclear components such as RNA, proteins, epigenetic markers etc…, giving a full comprehensive view of the genome, at the single cell level. Undoubtedly, exciting new data will emerge from these sequencing imaging technologies.
A paper[1] in Nature gives an overview of this emerging field and presents the most promising technologies to come.

1- https://www.nature.com/articles/d41586-022-00496-7