The 4D nucleome in Kraków - Prospects for an emerging field

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\textbf{ABSTRACT}

It may seem obvious that the structural complexity of the cell nucleus should be investigated by microscopy methods. However, the researchers’ toolbox has been enriched enormously in recent years by ideas arriving from a number of fields unrelated to microscopy. The recent conference 4D Nucleome: The Cell Nucleus in Space and Time, which was held in Kraków in May 2017, was an opportunity to appreciate the growing number of conceptual approaches and newly emerging analytical techniques that are revolutionizing our understanding of the structure of chromatin and the nucleus.

The conference “4D Nucleome: The Cell Nucleus in Space and Time” was held May 14–17, 2017 at the Jagiellonian University, Kraków, Poland (organizer: Jurek Dobrucki). The participants witnessed the rapidly advancing field of genome topography, driven by increasingly diverse and penetrative methods. Students’ textbooks convey an easily understood message: the cytoplasm is compartmentalized and functionally different regions are surrounded by biological membranes. These membranes are indispensable for maintaining specific functions underway in various organelles. It would be all too easy to transfer this notion to the cell nucleus - but for the fact that it has no membrane-bound substructures. There is an easily and always distinguishable nucleolus, however it stands out in phase-contrast microscopy because its optical properties differ significantly from the rest of the nucleus. Other than that it might seem that no unique subregions or specific chromatin structures are to be distinguished within the cell nucleus, whether in yeast or any other eukaryotic cell.

This way of thinking is proven incorrect when distinct regions of active replication or transcription, or subnuclear structures such as Cajal and PML bodies, are imaged by various microscopy methods. Functional identity of these regions is not maintained by membranes. Rather, the borders of these regions and their different contents appear to be maintained by mechanisms different than the ones that underly cytoplasmic membrane-based compartmentalization. Approaching these problems is contingent upon applying methods capable of identifying these subnuclear structures and investigating the mechanisms that define their functional and structural identity in the surrounding space filled with chromatin and various nuclear proteins and RNAs. All this had appeared elusive until recently and called for new methods of investigation.

While it would seem obvious that the structural complexity of the cell nucleus should be investigated by microscopy methods, the researchers’ toolbox has been enriched enormously in recent years by ideas arriving from several fields unrelated to microscopy. This recent conference in Kraków was an opportunity to appreciate the growing number of conceptual approaches and newly emerging analytical techniques that are revolutionizing our understanding of the structure of chromatin and the nucleus.

The meeting presentations included ones on single-cell applications of Hi-C chromosome capture (Peter Fraser), a novel genome architecture mapping method that complements Hi-C (Ana Pombo), CRISPR-labeling innovations for tracking chromosome dynamics (Thoru Pederson), biophysical dimensions of genome folding as
polymer topology (Angelo Rosa), the relationships of the 4D nucleome to gene readout (Hiroshi Kimura, Kerstin Bysticky, Noriko Saitoh) and DNA repair (Evi Soutoglou, Satoshi Tashiro, Magdalena Kordon). A masterful overview of emerging super-resolution microscopy (Christoph Cremer) reminded the audience that light has almost no limits now for revealing the genome as it dynamically resides in the nucleus. Nuclear dynamics including chromosome movement, TAD (topologically associating domain) formation, A- B- compartment formation, chromosome loop extrusion and other dynamics that were presented may contribute to compartmentalization inside the nucleus.

At the beginning of the meeting, the participants offered a moment of silence for the sad loss of Jörg Langowski, a pioneer of macromolecule biophysics and its applications to cell biology, including the nucleus.¹

At the closing session a quote by Sydney Brenner was mentioned: “Progress in science depends on new techniques, new discoveries and new ideas, probably in that order.” This was indeed a metaphor for this meeting. Building on momentum from previous 4D Nucleome meetings in Mainz, Germany, Hiroshima, Japan, the US and now the Krakow meeting, this growing international community now reaches a new chapter, full of promise in a shared spirit of bearing witness to a true paradigm shift in cell and molecular biology.

**Disclosure of potential conflicts of interest**

No potential conflicts of interest were disclosed.

**Funding**

J. D. is supported by National Science Center grant 2013/11/B/NZ3/00189, and N. S. by the JSPS KAKENHI 25116009 and 16H04744.

**Reference**

[1] Pederson T. Jörg Langowski- 1955–2017. Nucleus 2017; Jul 14:1–2. doi:10.1080/19491034.2017.1338087.