Statistical tools for analyzing nuclear features with preferred radial locations

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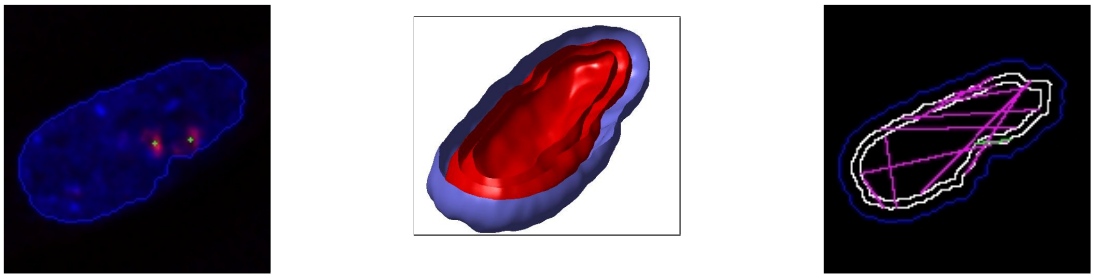
Many nuclear features (chromosome territories, nucleoli, loci) are not uniformly distributed within the cell nucleus and show a preferred radial location. The so-called erosion analysis based onto concentric 3D shells with constant volumes is commonly used for characterizing radial distributions. In [1], we introduced a variant of the erosion analysis with a continuous index called EVF (Eroded Volume Fraction). Using the EVF, one does not need to choose a discretization of the nuclear volume into shells and it is easier to detect small differences in radial locations. Furthermore, replacing shell-counts by the EVF makes it possible to use standard statistical analyses for quantitative data such as ANOVAs.

When several nuclear features show preferred radial locations, analyzing their spatial relations is not straightforward. As an example, in [3] we found that a gene cluster moved inwards when expressed together with an increase of RNA Pol II in its neighbourhood. However since RNA Pol II tended to be centrally located in the considered cell type, it was not obvious whether the increase of RNA Pol II could be entirely explained by the displacement towards the nucleus center. We addressed this question by introducing an original normalization of RNA Pol II intensity where the intensity at the gene cluster location is compared to all other intensities measured at nuclear locations with comparable radial positions. Using such normalized intensities, we were able to conclude that in addition to moving inwards the gene cluster had a tendency to get closer to RNA Pol II foci when expressed.

In [2], distances between chromosome territories (CTs) with preferred radial positions were analyzed. Comparing inter-distances between different pairs of CTs is not easy when the considered CTs have different preferred radial positions. Our approach was similar to the one described above. It was based on comparisons with inter-distances between simulated pairs of points drawn along *orbits*, see the figure below. Using this approach, it has been possible to show that the nuclear position of CTs is not ruled only by radial constraints. In particular, this was the case for two inner CTs which were closer than expected. It has been shown experimentally that both CTs were interacting with the central nucleolus.



Left: two CT's labelled in red. The CT centers are shown as green dots. Middle : the orbits associated with CT centers are surfaces at a constant distance from the nuclear boundary. Right: pairs of virtual CT centers were drawn at random along the orbits (magenta lines) and their inter-distances were compared with the inter-distance between the real CT centers (green line).

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2. C. Heride, M. Ricoul, K. Kiêu, *et al.* Distance between homologous chromosomes results from chromosome positioning constraints. *Journal of Cell Science*, 123(23):4063–4075, 2010.

3. C. Kress, K. Kiêu, S. Droineau, *et al.* The casein gene cluster colocalizes with RNA Pol II nuclear domains in luminal mammary epithelial cells. Submitted, 2011.