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Computational Approaches for 2D and 3D Modeling of the Macro-Architecture of Native Chromosomes in Sperm Genome of Drosophila Melanogaster

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As a first justified concept over 125 years of the history of the basic scientific ideas on the large-scale arrangement of eukaryotic interphase chromatin in cell nucleus, 2D and 3D spatial macro-architecture of haploid chromosomes in Drosophila sperm nucleus was sequentially reconstructed using the detected non-random distribution of γ-ray- and neutron-induced inversion and translocation breakpoints along the euchromatic chromosome maps with their clastering around heterochromatin.

Key words and phrases: interphase chromosome, spatial configuration, 2D and 3D models, sperm genome, Drosophila.

1. Introduction

Keeping in mind the conceptual Bennett's [1] statement that "...the simple haploid genome is a basic structural unit in nuclear architecture" and, then, the fact that his question " ...what of ordered arrangements within this unit?" still remains to be solved, we have investigated the global arrangements of chromosomes in haploid *Drosophila* sperm genome using the experimental data obtained on the non-random patterns of radiation-induced locus-specific intra- and interchromosomal exchanges (inversions and reciprocal translocations, respectively). The formation of such exchanges is known to require that the two interacting chromosome regions with breaks were spatially close to each other enough.

Therewith, our radiation-genetic experiments were designed so that to isolate not all of possible randomly arising in sperm genome irradiated chromosome exchanges but only those that have had one of inversion or translocation breaks (the so-called "first break") invariably associated with one or another selected genetic loci of different location on the large autosome 2 (black body – "*b*" or vestigial wings – "*vg*"). Then, location of the second inversion/translocation breaks should indicate which chromosome regions, and as often in different sperm nuclei, are spatially close to the gene-reporters selected showing thereby the loops of appropriate sizes. Therefore, large enough sets of gene-specific exchanges can give on insight into the global loop arrangement and topographic parameters of chromosomes under study in haploid sperm nucleus. Using this approach,large sets of γ-ray- and neutron-induced locus-specific inversions [2, 3] and translocations [4] were obtained and the positions of the second inversion/translocation breakpoints were precisely determined by the standard cytological technique for *Drosophila* polytene chromosomes.

As the cytological data and statistical analysis have shown, the distribution patterns of the second exchange breakpoints along the entire chromosomes 2 and 3 under study were highly non-random clustering within some specific for two gene-reporters "hot" euchromatic regions and in heterochromatin complex as well (Fig. 1). This picture suggests the putative megarosette-loop configuration for both two large chromosomes (from three ones) in Drosophila sperm genome.

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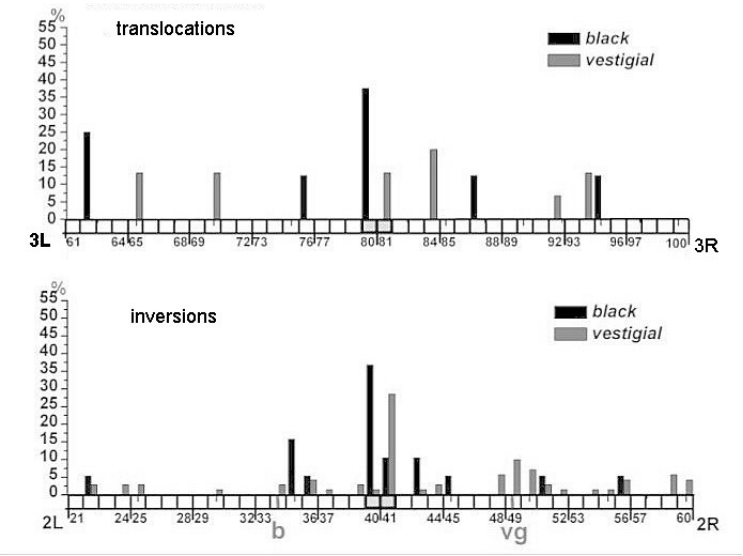

Figure 1. **Relative frequency and distribution patterns of translocation (up) and inversion (below) breakpoints along the entire chromosome 3 and 2, respectively, for the b- and vg-specific exchanges induced by gamma-ray and neutrons in Drosophila sperm genome**

2. Methods

For modeling and visualization of such an unusual configuration, some approaches for using a software program complex for 2D and 3D modeling [5–7] were elaborated. As a first step, a 2D model was constructed as B spline comprising of 40 standard chromosomal sections for each chromosome. Among them, the sections with inversion /translocation breakpoints were moved closer to the heterochromatin complex and two chromosome regions with the gene-markers which often interact each other over distance $L = \sqrt{N}$ (N — the number of inversion and translocation breakpoints detected) at $L_{\min} = 4$ nm. In this model, each section occupies 9 degrees of a circular expansion relative to the centre with the gene-markers. Then, numerous refinements of the model have been introduced so the chromosome sections in the 3D model do not cross each other within the volume of the cell nucleus. Therewith, the chromosome sections without breakpoints were constructed as a "giant" relaxed loops on periphery of this nucleic volume.

At the final step, knotty primitives are arranged at regular intervals along the line of the spline obtained. Lastly, coloration and labeling of chromosome sections as well as choice of the model illumination were carried out sequentially.

3. Result

As a result, the reconstructed spatial configurations of haploid chromosomes in *Drosophila* sperm nucleus are defined as highly specific and universal for all large chromosomes megarosette-loop structures having unitary heterochromatic compartment. A general 2D and 3D models designed are presented at Fig. 2 and Fig. 3, respectively.. These structures are radically distinct from the linear-polar Rabl's configuration of interphase chromosomes in animal and plant somatic cells [8] bearing witness to high specificity of molecular-biological mechanisms of self-organization of germ cell haploid genome during post-meiotic stages of its differentiation from earlier spermatids to mature sperms.

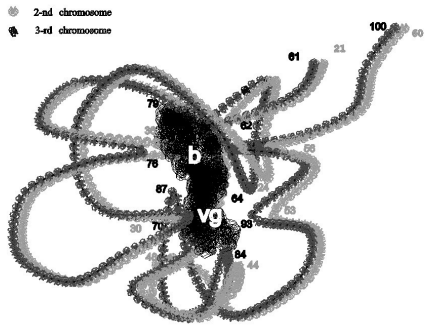

Figure 2. **An example of a general 2D models for both *Drosophila* autosomes 2 and 3 as an unitary entity based on "hot" inversion/translocation breakpoints. Black body - the heterochromatic compartment; the b and vg - gene-loci which mark the putative "sensitive" microvolumes in spatial proximity relative to heterochromatic compartment; the number 21...60 and 61...100 denote the relevant sections of autosome 2 and 3, respectively**

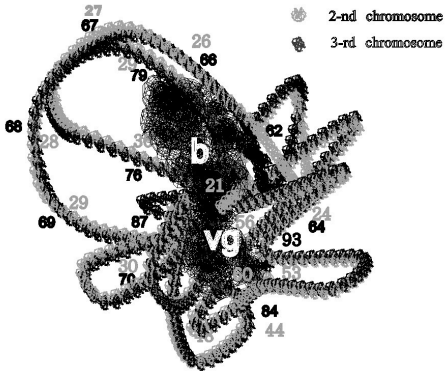

Figure 3. **An example of a general 3D models for both *Drosophila* autosomes 2 and 3 based on extra inversion breakpoints. (Symbols are the same as in Fig.2)**

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Компьютерные подходы к 2- и 3-мерному моделированию макро-архитектуры интерфазных хромосом в геноме спермиев Drosophila melanogaster

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Впервые за 125-летнюю историю научных идей о пространственной организации интерфазных хромосом в ядре клеток высших эукариотов представлена экспериментально обоснованная 2- и 3-мерная компьютерная модель макроархитектуры гаплоидных хромосом в геноме спермиев D.melanogster, компактно уложенных в виде мегарозеточно-петлевых образований, на что указывает неслучайное распределение индуцированных гамма-лучами и нейтронами инверсионных и транслокационных точек разрывов по длине хромосом с их кластеризацией вокруг гетерохроматинового комплекса внутри ядра.

Ключевые слова: интерфазные хромосомы, пространственная организация, двух- и трехмерные модели, геном спермиев, дрозофила.