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Higher order structure of mitotic chromosomes

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From observations on the partial disintegration of mitotic chromosomes isolated from human fibroblasts we propose that human mitotic chromatids are characterized by a rather simple organization based on the folding and coiling of a long, regular, hollow cylindrical structure the *unit fibre*, with a diameter of about 400 nm (Bak, Zeuthen & Crick 1977). This structure is postulated to consist of a *super-solenoid* formed by the coiling of the 30 nm solenoid (itself formed by coiling of the string of nucleosomes). We therefore suggest the human chromatid to be contracted in a hierarchy of helices, with contraction ratios of the DNA molecule corresponding to each level of coiling being 7 (string of nucleosomes), 6 (30 nm solenoid) and 40 (400 nm supersolenoid); in addition we envisage further contraction by a factor of about 5 due to coiling of the super-solenoid fibre. The result of these contractions is an overall packing of DNA in the same order of magnitude as calculated from the length of a chromatid and its DNA content. The lengths of the fibres isolated from human fibroblasts range between 11 and 56 μm. The length distribution represents a number of peaks which agree, with respect to their relative lengths, with the relative DNA contents of the human chromosome set. To study if similar structures are a general feature of chromosome structure we have also recently studied isolated chromosomes of mouse C1–1D cells or mouse embryo fibroblasts and of *Drosophila* E85 cells. When mitotic mouse cells were treated in chromosome buffer, chromosomes disintegrated like human chromosomes, although more slowly. The dimensions of the unit fibres, from mouse mitotic cells were similar to those of the human fibres with a diameter of about 400 nm, and no statistically significant difference in the measured diameters of human and mouse fibres was found (Bak, Bak & Zeuthen 1978). Chromosomes were also isolated from the *Drosophila* E85 cell line ($2n > 90\%$, XX; XO), and mitotic chromosomes from these cells disintegrated into unit fibres which also in this case had an average diameter of about 400 nm. The length distribution showed three clearly defined peaks of 11, 13 and 15 μm, respectively which could correspond to the three larger chromosomes in the haploid chromosome set of *Drosophila* (Zeuthen, Bak & Bak 1978). The molecular mass of the largest chromosomal DNA in *Drosophila* has been determined directly as $41 \pm 3 \times 10^9$ (Kavenoff & Zimm 1973), which corresponds to a length of 2×10^4 μm. Using this figure and the length of the longest unit fibres isolated from the *Drosophila* cells we arrive at a factor of about 1400 as our best direct estimate of the contraction of DNA within the unit fibre.

Since unit fibres of about 400 nm diameter were found both in isolated human, mouse and *Drosophila* chromosomes, we propose that super-solenoids could be a general feature of chromosome organization. As mentioned, we envisage that the unit fibre must be contracted by a further factor of 5 to allow for the final contraction of DNA in the chromatid. The main problem which remains is whether this folding is in the form of a single helix or in the form of a double helix. Many of our unit fibres are folded to give the impression of a folded loop, but

as we previously have pointed out (Bak *et al.* 1977), such a folded model, although suggested by the appearance of many of our unit fibres, is hard to accept in relation to a number of known genetic phenomena and could be due to aggregation. We therefore favour a single helical coiling of the unit fibres to give the final coiling by a factor of 5, and are currently trying to obtain more conclusive data to illuminate this question.

References (Bak & Zeuthen)

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