Supplementary Figure 1

(a) The location of sliding windows may have an impact on the ability to detect small CNVs. The black lines schematically display a heterozygous deletion, the red lines represent windows used for the calculation of the mean ratio value for the respective region. Windows within the deletion or at least partly within the deletion are shown in light red. The blue line exhibits the ratio profiles generated based on the mean values of the windows above.

(b) Our algorithm calculates the mean ratio value for each window; this value is not assigned to the entire window (as in Supp. Fig. 1a) but only to the center position of the respective window (Supp. Fig. 1b, blue dots). In the depicted example windows were once moved to different locations and the calculations were repeated. The small blue squares depict the corresponding ratio values.

(c) Comparison of the ratio profiles of proband P2 of the non-amplified DNA (upper panel) with the ratio profile of the 10 cell pool (lower panel). For details see Material and Methods.

Supplementary Figure 2

(a and b) Depending on the window sizes different regions may be called as over- or underrepresented, as illustrated by two calculations done with the 10 cell pool of proband P2. The calculation shown in (a) was made with fixed window size of 500 oligos (32.5 kb) whereas for the calculation in (b) window sizes of 2.500 oligos (162.5 kb) were used (for details see Material and Methods).

(c) Generation of specific patterns of calls for under- or overrepresented regions generated with various window sizes. Panel (1): Four different calculations, each with different window sizes. Panel (2): If a window shows a significantly increased or decreased ratio

value the mean position of the window will be displayed above or below the respective region. Depending on the window size it will be labeled with a different color and distance to the X-axis, so that a color bar code is generated. Panel (3): The color bar code is helpful in estimating the size of a CNV, because the smaller the CNV the less color bars will be generated. Panel (4): Some bar code patterns should not occur and demonstrate that identified gains and losses are more likely to be artifacts. As illustrated on the left side, it should not occur that there are no calls at the smallest windows and that CNVs are only noted at larger window size. Calls should be uninterrupted or continuous, thus there should be no gap between calls of two different window sizes (center). A single call at any window size, with the exception of the smallest window, is certainly an artifact (right).

Supplementary Figure 3

The ratio profile of proband P2 on the custom-made Agilent chromosome 22 tiling array calculated with the algorithm described in this manuscript. The center profile is again based on calculations with window sizes of 100 adjacent oligos (corresponding to 10.4 kb on this array platform). In contrast to the NimbleGen arrays, gains and losses are displayed reversed, i.e. deletions below the X-axis in red and gains above the X-axis in green.

Supplementary Figure 4

Cell pool results obtained for proband P2 on the Agilent custom made Chromosome 22 array.

(a) Evaluation of the 10 cell pool on the Agilent Chromosome 22 array allowed only the identification of the 3 Mb deletion. The center profile was obtained with a window size of 5.000 adjacent oligos (corresponds to 520 kb).

(b) On the Agilent Chromosome 22 array we again obtained a similar result with the 5 cell pool, i.e. identification of the 3 Mb deletion. The center profile was calculated with the same values as used for the 10 cell pool.

Supplementary Figure 5

Chromosome 22 result for proband P2 obtained with the same single cell amplification product as shown in Fig. 4. The 3 Mb deletion is detected again.

Supplementary Figure 6

(a) Comparison of hybridization patterns obtained with non-amplified DNA of proband P1 on the NimbleGen Chromosome 22 Tiling array (upper panel; 100 oligo windows) and on the 2.1 M Whole Genome array (lower panel; 50 oligo windows). The hybridization patterns between these two platforms only show some minor differences. On the 2.1 Mb Whole Genome array there are some regions at positions 18 Mb to 20 Mb, in addition to the 2.8 Mb deletion, which have ratio values consistent with deletion and are therefore displayed in green. Furthermore, the proximal chromosome 22 region appears to be duplicated (red region). This reflects different oligo representations on these two array platforms. Chromosome 22 has some regions with highly repetitive sequences which were omitted on the Chromosome 22 Tiling array and are therefore visible as gaps on this array platform (see upper panel). In contrast, these regions are represented on the 2.1 M array and are hence prone to ratio deviations.

(b) Chromosome 22 ratio profile obtained with the 10 cell pool of proband P1 on the 2.1 M whole genome array, the 2.8 Mb deletion is clearly visible. An additional region at position 21 Mb with the size of about 750 kb also appears to be deleted. This is, however, not the same region which had been shown as potentially deleted on the Chromosome 22 Tiling

array (compare Fig. 5a). Here a 2.500 oligo sliding window (corresponding to 2.35 Mb) was used for the center profile.

(c) Ratio results obtained with the 5 cell pool in which the 2.8 Mb deletion can also be detected with ease. This image represents a particularly good example for distinguishing between real CNVs and artifacts: using the 2.500 oligo window a deletion at 32 Mb and a gain in the proximal 22q region would have been identified as shown by the cyan bars. As the profile in the center was also obtained with a 2.500 oligo window the corresponding parts of the ratio profile are illustrated in red and green, respectively. However, neither region was called with any of the smaller windows, revealing that these are most likely to be merely artifacts, which is in fact the case.

Supplementary Figure 7

Identification of the 2.8 Mb deletion in single cell #1 of proband P1 on the 2.1 M whole genome tiling array. Once more, the bar code pattern demonstrates that possible deletions at 25 Mb or 33 Mb are in fact artifacts. The profile in the center was obtained with a 2.500 oligo sliding window (corresponding to 2.35 Mb).

Supplementary Figure 8

Ratio profiles of the X-chromosome.

(a) X-chromosome hybridization pattern obtained with non-amplified DNA of proband P1 on the 2.1 M Whole Genome array. The location and size of X-chromosome landmarks is shown.

(b) X-chromosome evaluation of the single cell #2 from proband P1. In this cell the deletion on chromosome 22 was not identified.

(c) X-chromosome evaluation of the single cell #3 from proband P1. In this cell the deletion on chromosome 22 was not identified.

Supplementary Figure 9

Copy number changes identified in cell line 796P:

(a) Array-CGH profile obtained with non-amplified DNA.

(b) One exemplary array-CGH profile generated from a single-cell.

Supplementary Figure 10

Array-CGH profiles obtained with cell line HT29:

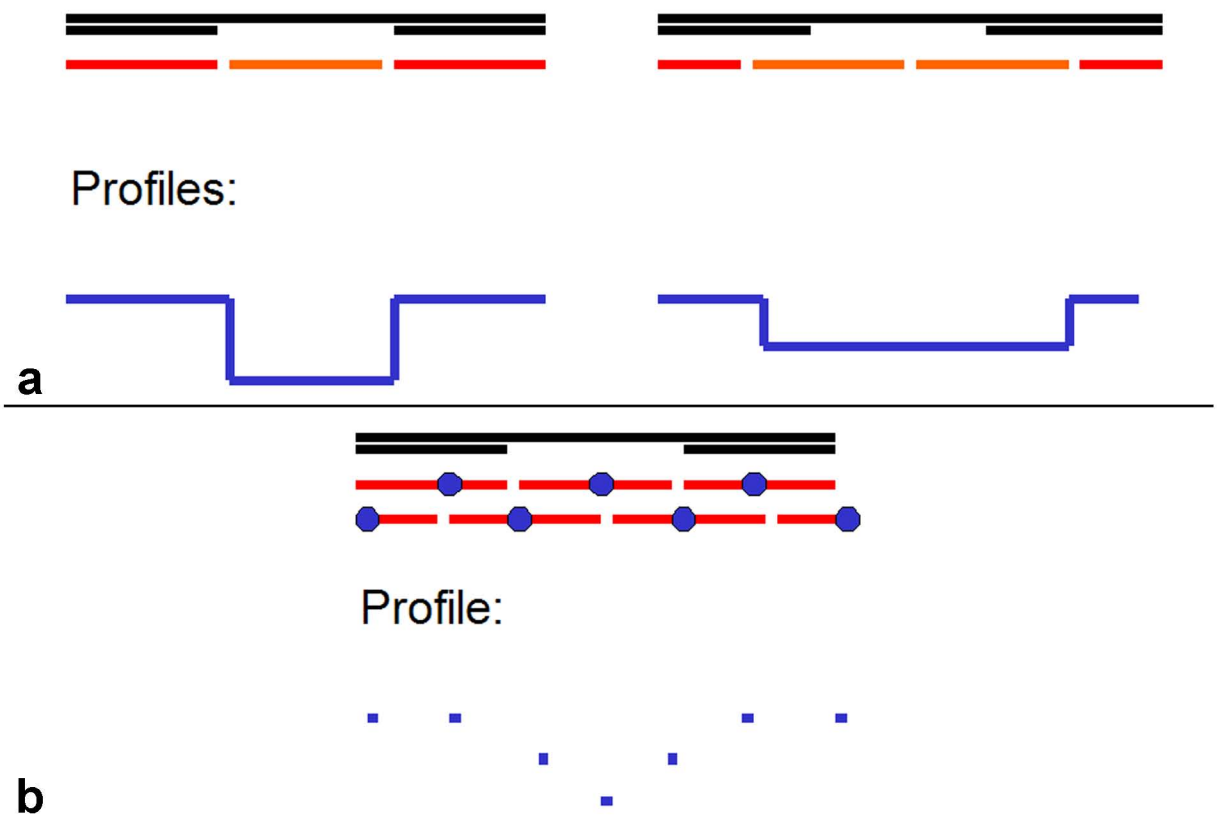
(a) Array-CGH profile acquired with non-amplified DNA.

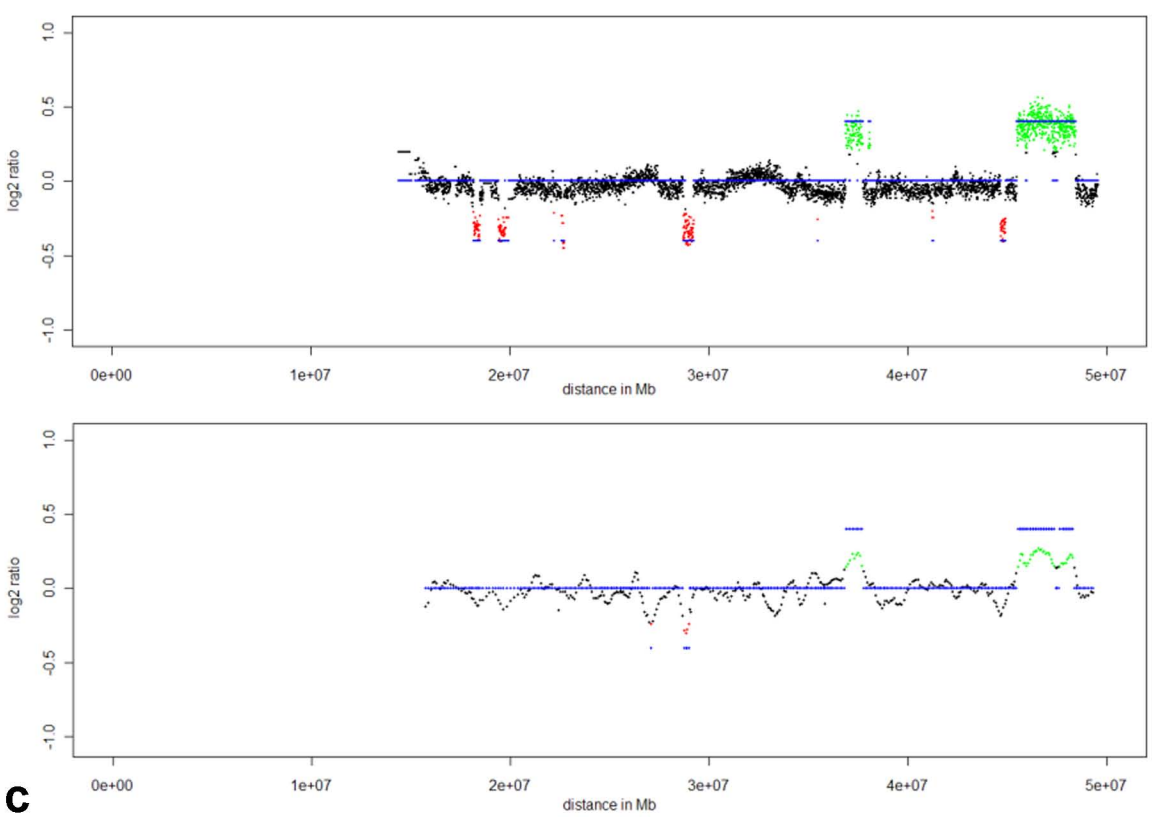
(b-e) Four array-CGH profiles calculated from different single-cell amplified cells.

Supplementary Figure 11

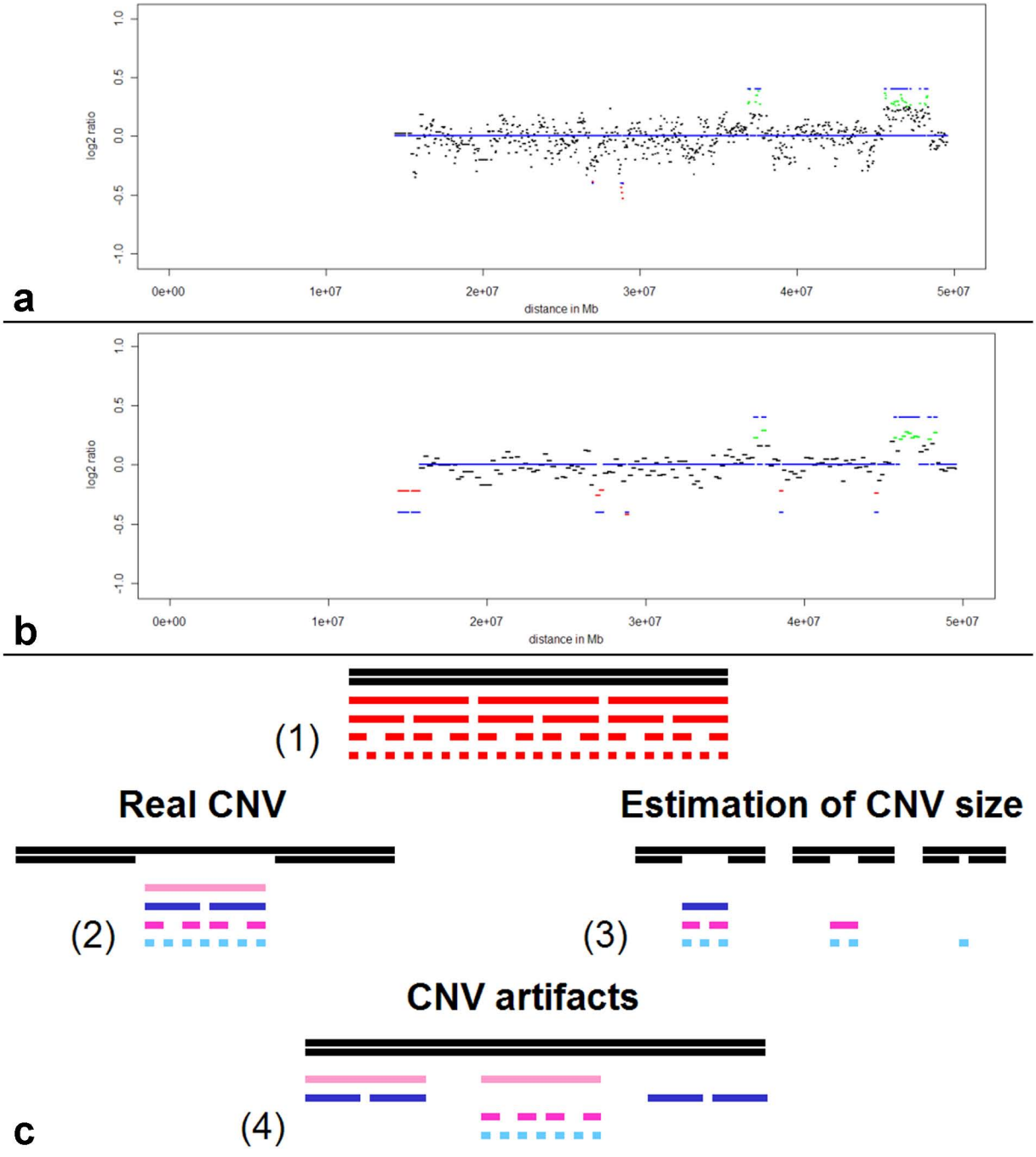
Matching first (a) and second (b) polar bodies with complementary gains and losses for chromosomes 1, 9, 10, 13, 18, 20, and 21. In addition, the first polar body (a) has a gain of chromosome 14, the second polar body additional gains of chromosome 17 and losses of chromosomes 2, 3, 4, 6, 7, 11, and 15.

Supplementary Figure 1

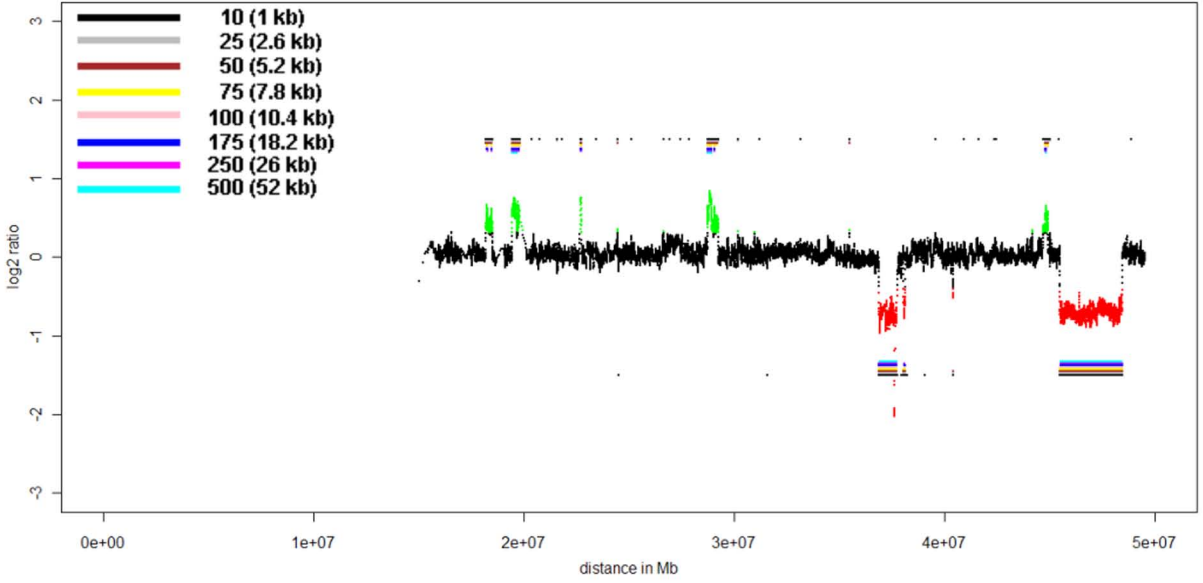




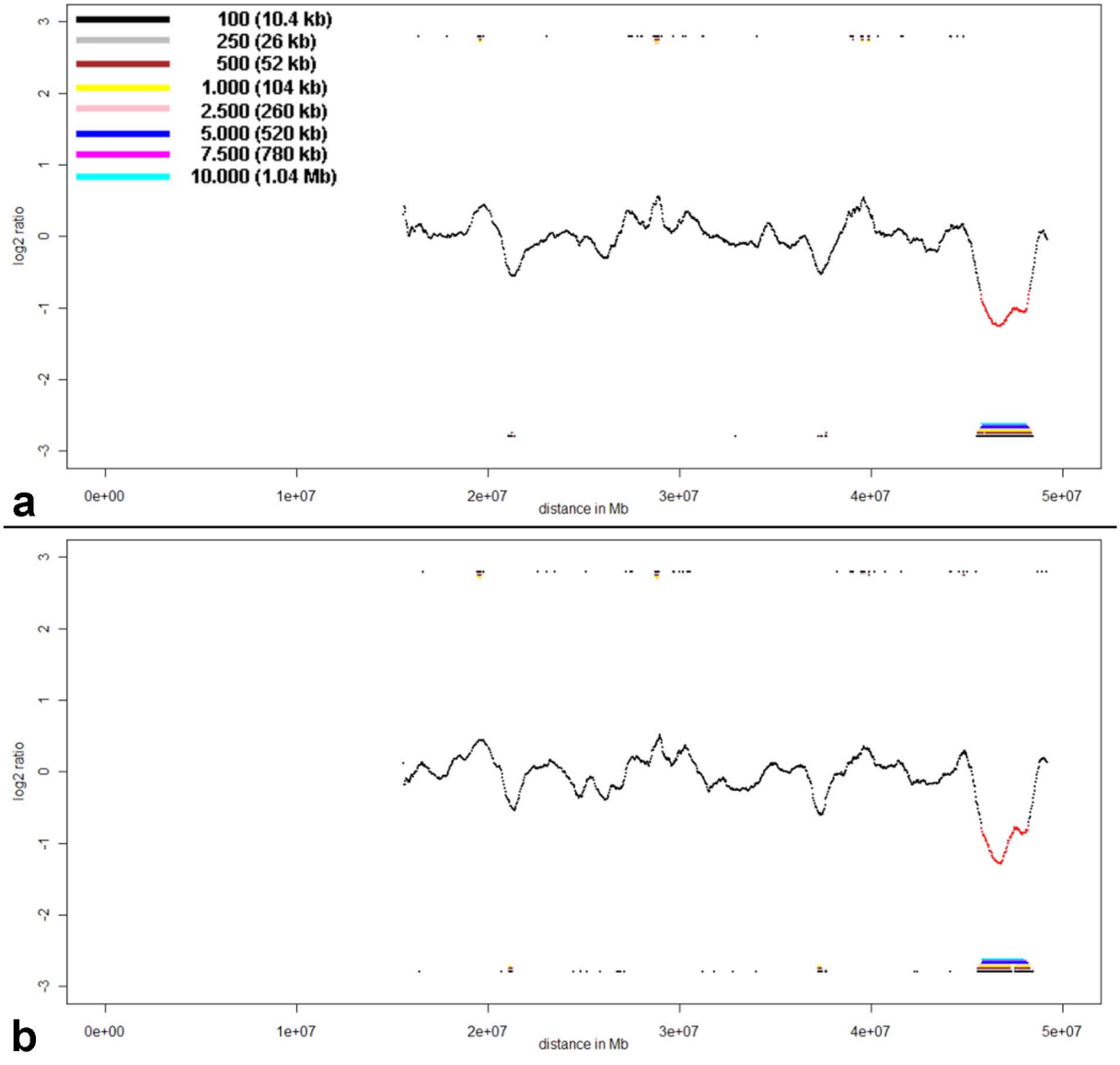
Supplementary Figure 2



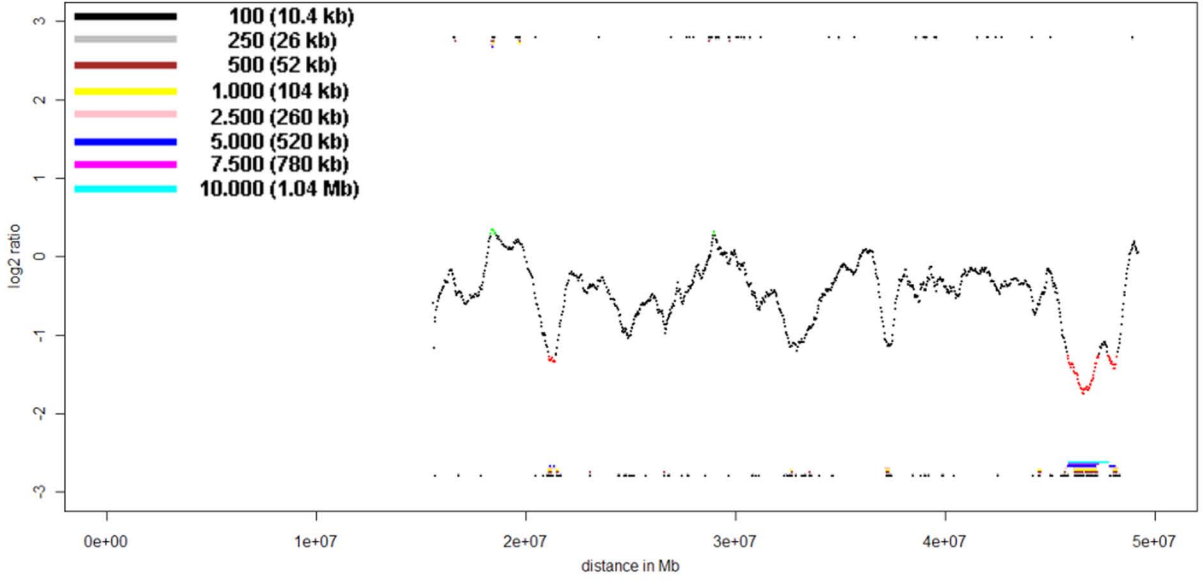
Supplementary Figure 3



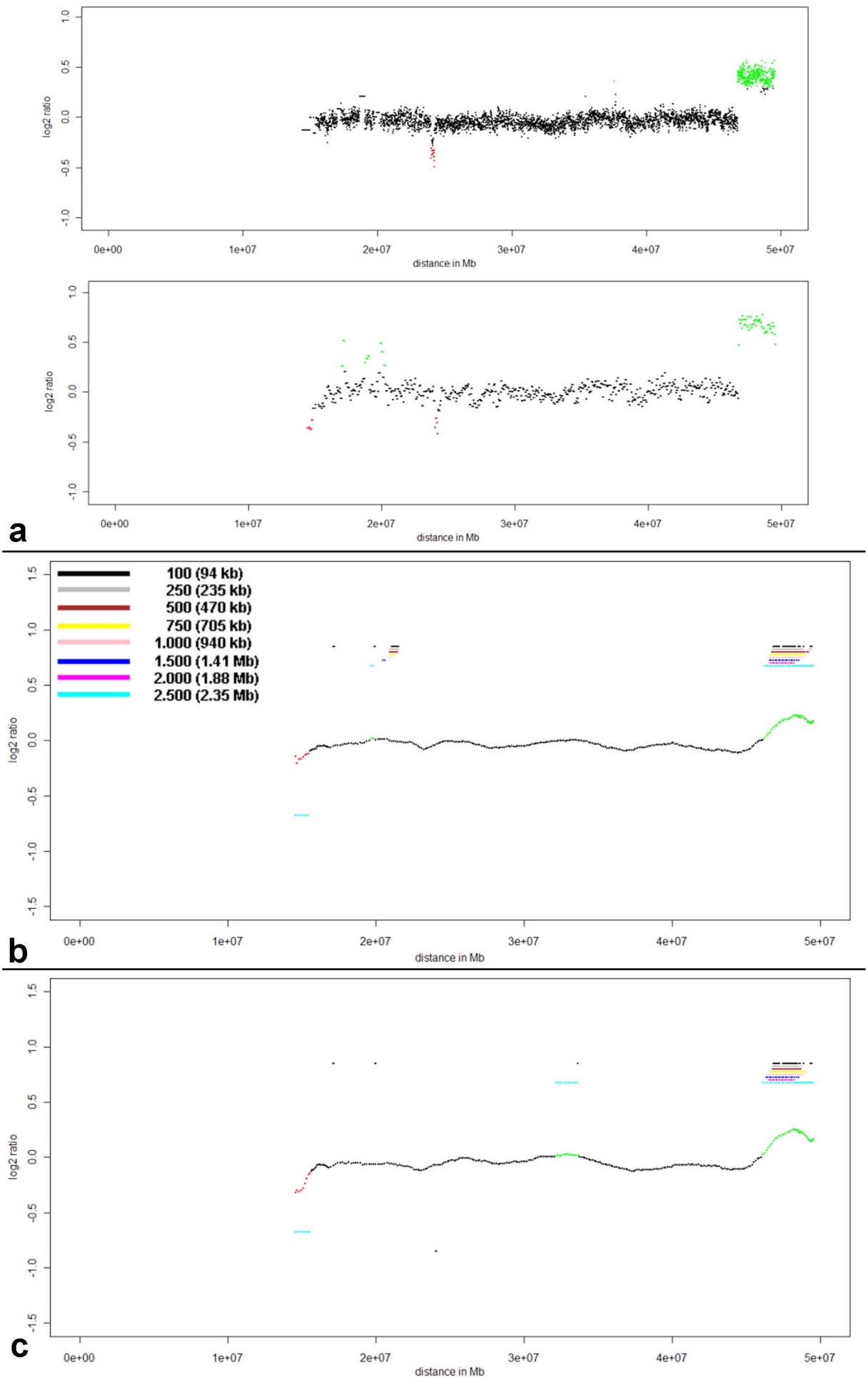
Supplementary Figure 4



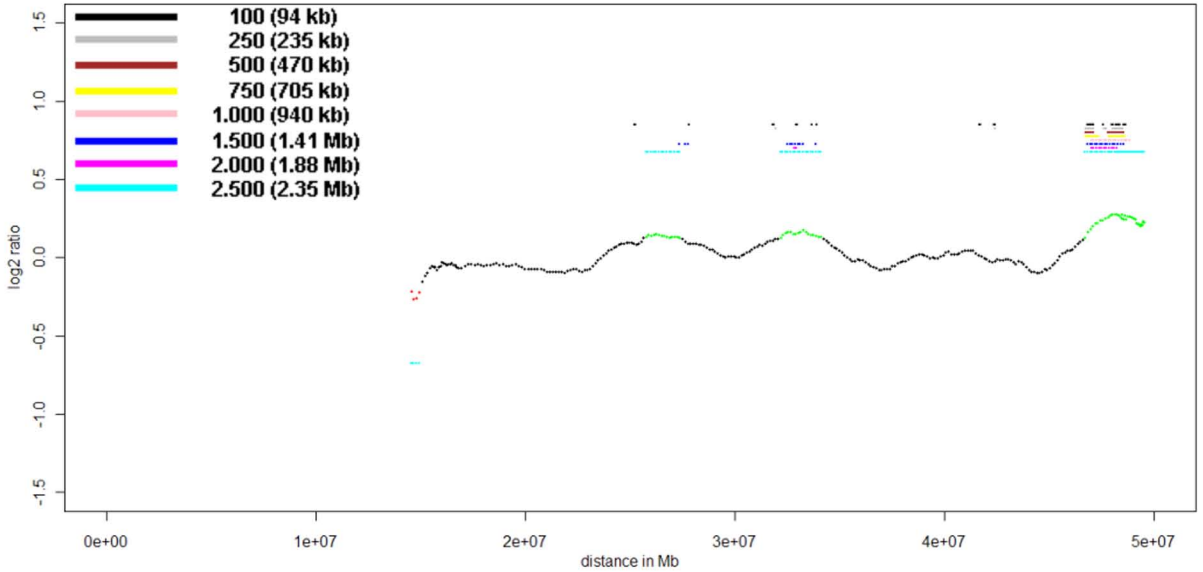
Supplementary Figure 5



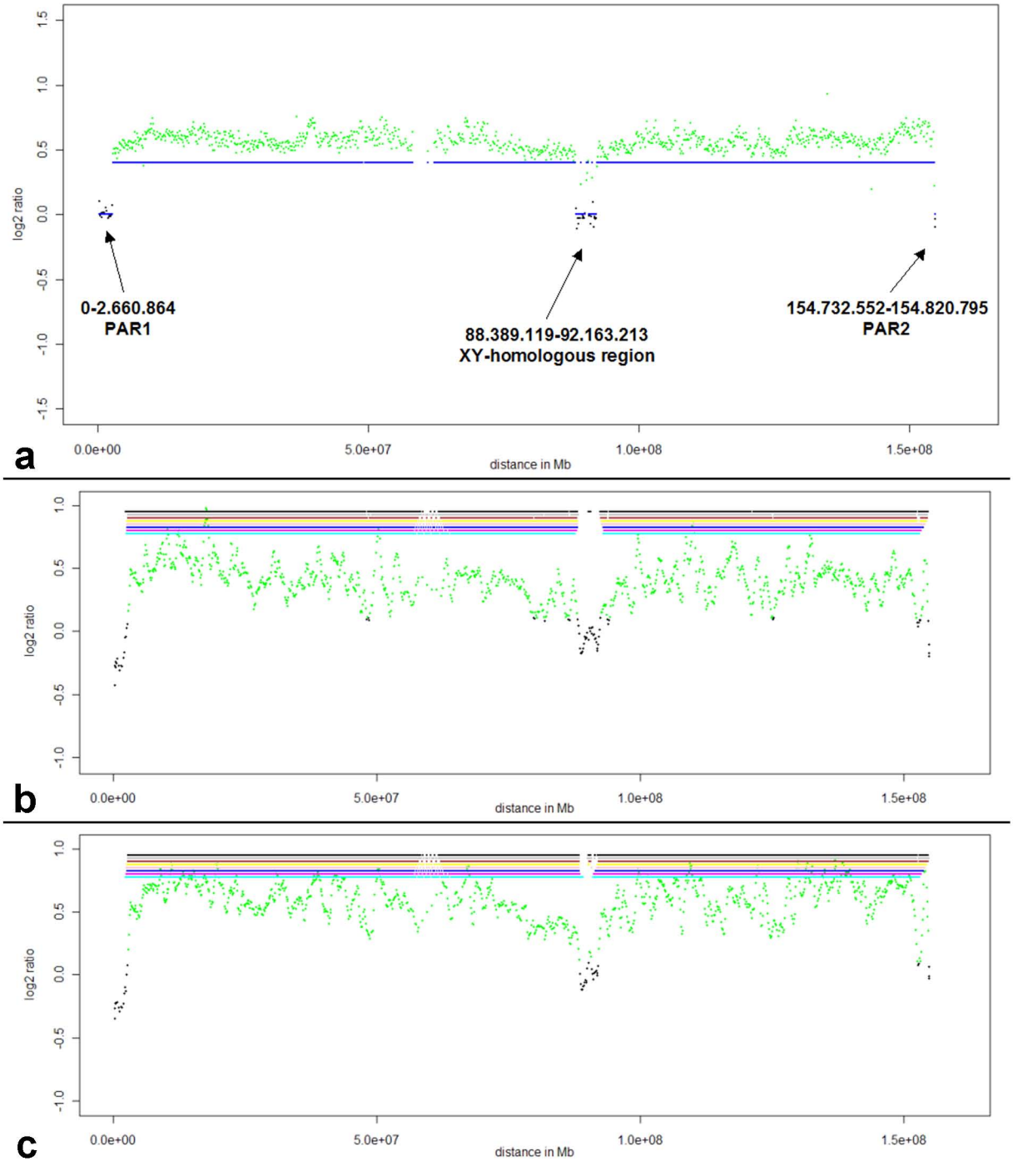
Supplementary Figure 6



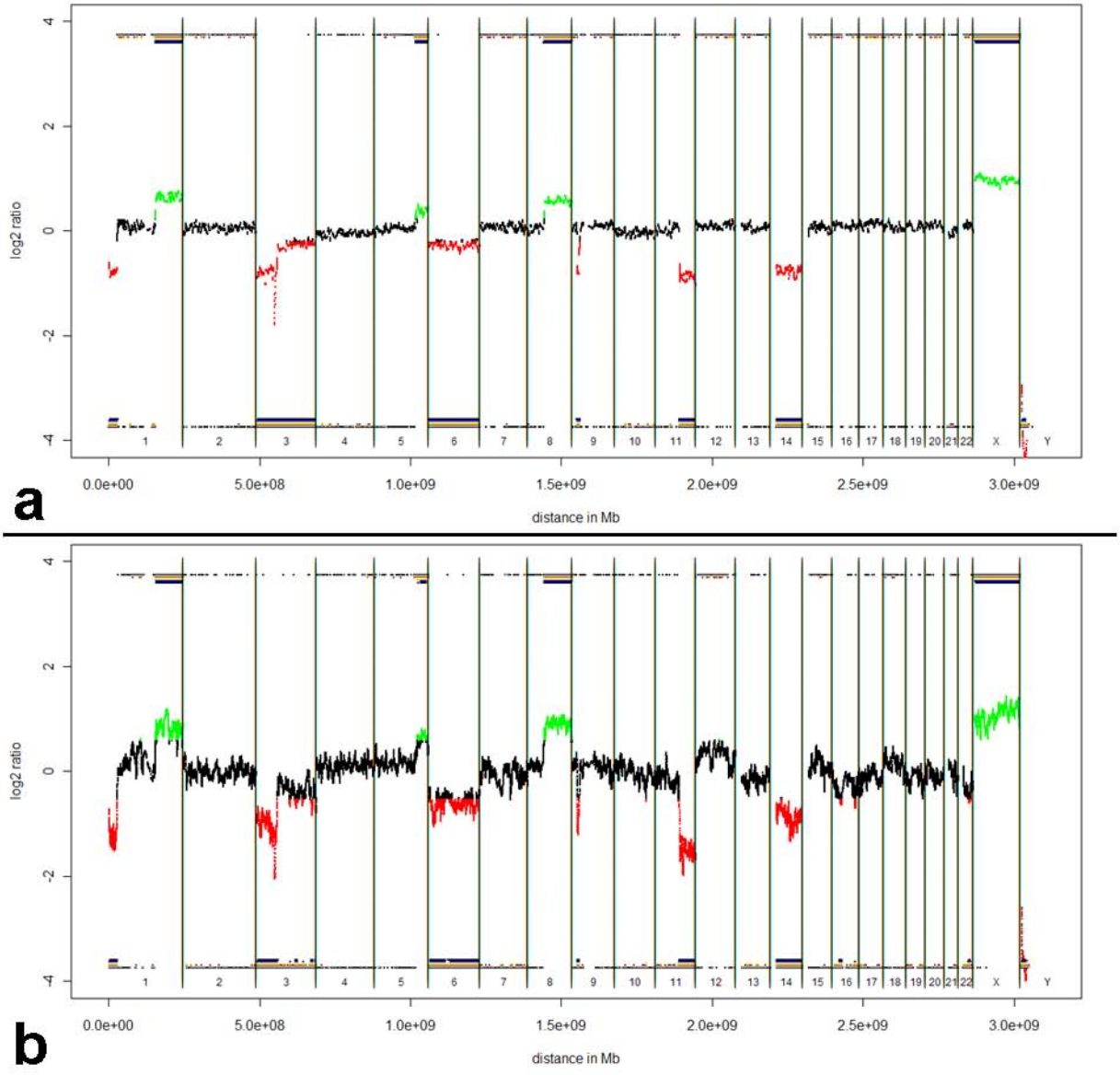
Supplementary Figure 7



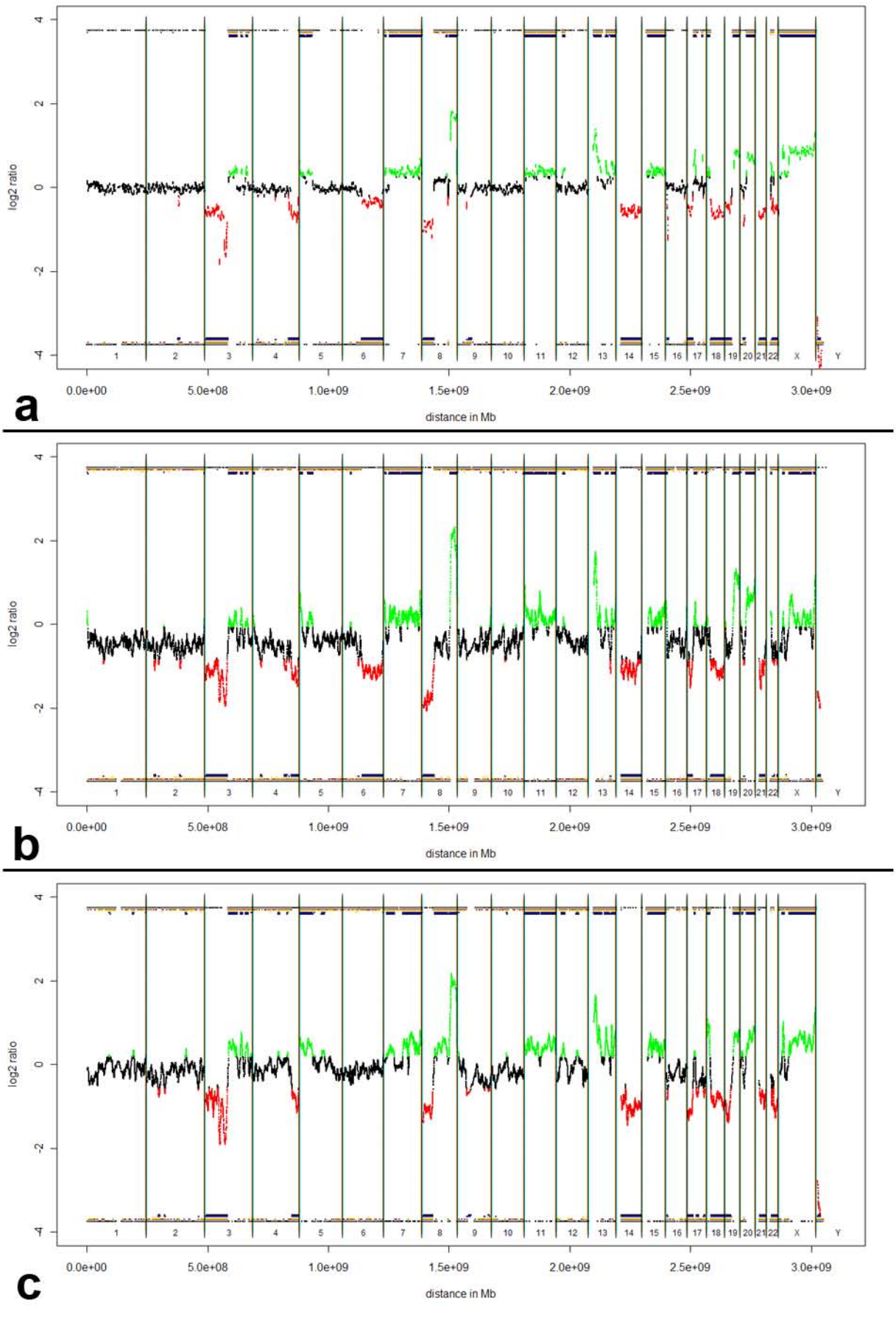
Supplementary Figure 8



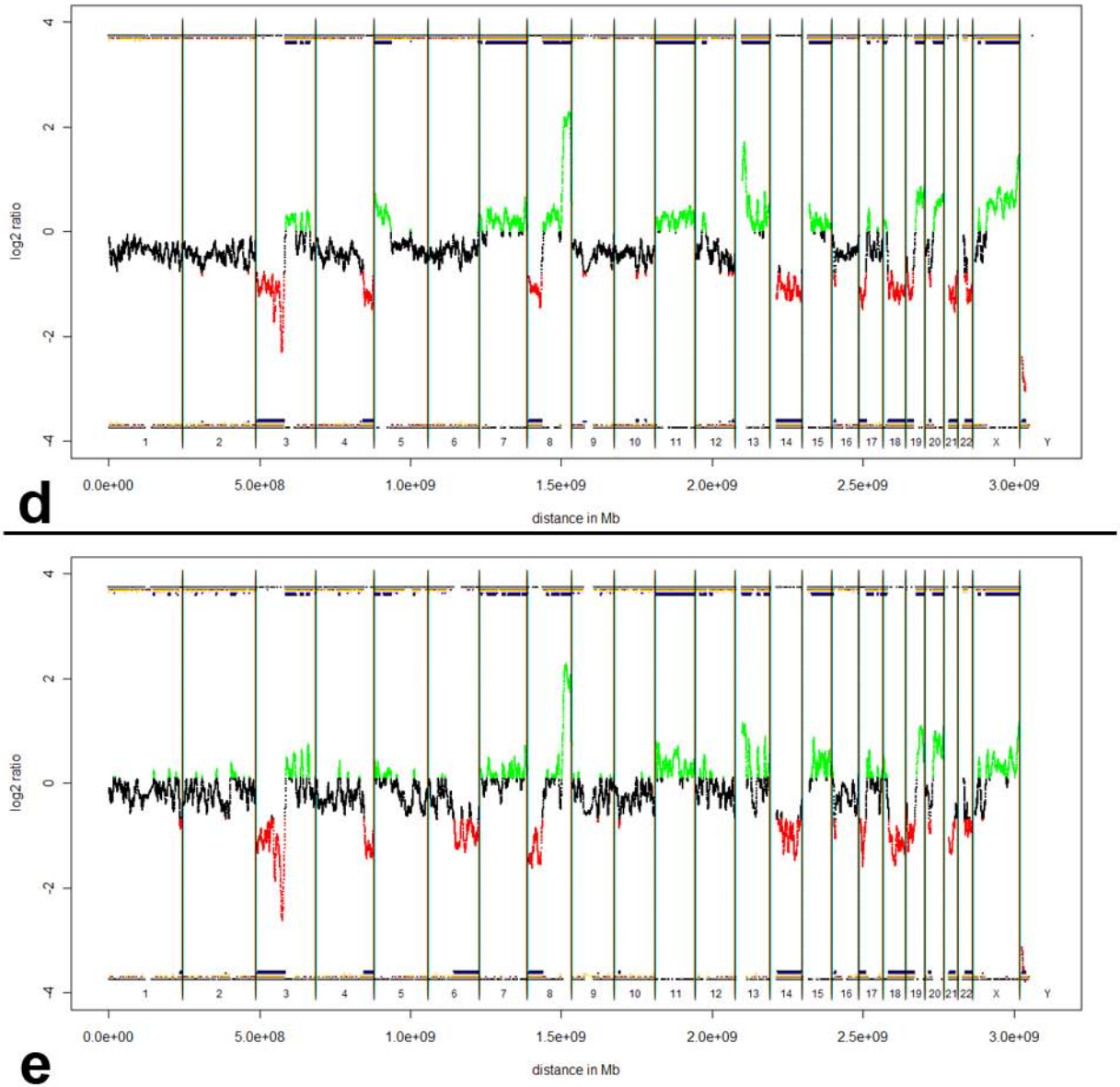
Supplementary Figure 9



Supplementary Figure 10



Supplementary Figure 10



Supplementary Figure 11