



### Supplemental Figure S1.

- a. Changes in the number (top) and the mean size (bottom) of domains between when the threshold RI value is increased by 5% with respect to the x coordinate of the data point (i.e. the point at 60% represent changes when increasing from 60% to 65% etc).
- b. Normalized mean size (upper panels) and number (lower panels) of domains as a function of the minimal RI threshold used to define them (semi-log scale), in NPC, CH12 and ESC. The normalized number of domains detected in regions belonging exclusively to either the A and B compartment is shown for ESCs. Normalized number of domains genome-wide for ESC is plotted in main Figure 1c.
- c. Cumulative distribution of the size of domains at 55% (median 180 kb).
- d. Fraction of domains with at least one CTCF bound site at both boundaries, as a function of the RI used to define domains. Straight lines indicate domains whose size is most similar to contact domains (7).
- e. Fraction of boundaries of contact domains in CH12 cells (7), which are detected by the CaTCH algorithm applied to same Hi-C dataset, as a function of the RI used to define hierarchical domains. Maximal overlap is found at 62% RI.
- f. Example of domains at 62% of RI in CH12 (black lines) and contact domains (7) (green lines) for a small region of chromosome 19 in CH12 cells.
- g. Number (left panel) and mean size (right panel) of domains detected by the directionality index method (diTADs) (7) as a function of the “window size” parameter required by the method. No intrinsic rule allows to choose any window size below 8 Mbps from these plots.
- h. Cumulative distribution of domains size for diTADs (red curve) and domains at 69% RI (blue curve). KS-test shows that these two sets of domains are not significantly different.
- i. Example of domains at 69% of RI (black squares) and diTADs (green squares) for a small region of chromosome 19 in ESCs. The CaTCH algorithm is more sensitive to small variations in contact probabilities within large, uniform domains.
- j. Pie chart representing the properties of non-conserved domains between diTADs and the set of domains at 69%. Most domains at 69% divide a diTAD into smaller domains.
- k. Enrichment in correlation of histone marks within vs. across domains (7). Correlation is maximal at the scale of compartments, consistent with the notion that compartments A and B represent stretches of active and inactive chromatin respectively.
- l. Right: Number of domains detected by CaTCH as a function of RI in computationally generated contact maps with one preferential folding level and different domain sizes. Left: The corresponding heat map.