Human Fibroblast IMR90 Hi-C Data (Dixon et al.)

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1 Introduction

The Hi-C technic was first introduced by Lieberman-Aiden et al. [2009]. In the continuity with 3C, 4C and 5C technics, the goal of the Hi-C is to simultaneoulsy detect all chromosomal contacts in a single experiment. All this technics aim at measuring the population-averaged frequency at which two genomic loci physically interact in three-dimensional space. In Hi-C, after a first crosslink and digestion, all genomic fragments are labeled with a biotinylated nucleotide before ligation. These junctions can then be purified efficiently by streptavidin-coated magnetic beads, and finaly sequenced using a standard Illumina paired-end protocol.
The data available in this package were published by Dixon et al. [2012] and downloaded from the GEO website (GSE35156, sample GSM862724). This publication is one of the key paper in the field for two main reasons: i) it was the first time than Hi-C data were generated at such resolution (up to 20kb), ii) this resolution highlighted a new short range structure defined as topological domains (TADs), with high frequencies of intra-domain chromatin interactions but infrequent inter-domain chromatin interactions (Nora et al. [2012]).

If you use *HiCDataHumanIMR90*, please cite:

- Servant N (2014). HiCDataHumanIMR90: Human Fibroblast IMR90 HiC data from Dixon et al. 2012. R package version 1.1.0.
- Dixon JR, Selvaraj S, Yue F, Kim A et al. (2012) Topological domains in mammalian genomes identified by analysis of chromatin interactions. Nature 485(7398):376-80.

2 Hi-C Data

The `hic_imr90_40` object is a *HTClist* object (see the *HiTC* package for more information (Servant et al. [2012])). It contains the complete genome-wide HiC data, with all inter and intrachromosomic contact maps at a resolution of 40kb.

```
> require(HiCDataHumanIMR90)
> require(HiTC)
> data(Dixon2012_IMR90)
> ## Show data
> show(hic_imr90_40)
```

```
HTClist object of length 325
25 intra / 300 inter-chromosomal maps
```

```
> ## Is my data complete (i.e. composed of intra + inter chromosomal maps)
> isComplete(hic_imr90_40)
```

```
[1] TRUE
```

```
> ## Note that a complete object is not necessarily pairwise
> ## (is both chr1-chr2 and chr2-chr1 stored ?)
> isPairwise(hic_imr90_40)
```

```
[1] FALSE
```

```
> ## Which chromosomes ?
> seqlevels(hic_imr90_40)
```

```
 [1] "chr1"  "chr2"  "chr3"  "chr4"  "chr5"  "chr6"  "chr7"  "chr8"  "chr9"  "chr10"
[11] "chr11" "chr12" "chr13" "chr14" "chr15" "chr16" "chr17" "chr18" "chr19" "chr20"
[21] "chr21" "chr22" "chrX"  "chrY"  "chrM"
```

```
> ## Details about a given map
> detail(hic_imr90_40$chrXchrX)
```

```
HTC object
Focus on genomic region [chrX:1-155270560]
CIS Interaction Map
Matrix of Interaction data: [3882-3882]
Binned data - window size = 40000
3882 genome intervals
Total Reads =  15349610
Number of Interactions =  3362484
Median Frequency =  1
Sparsity =  0.112
```

```
> ## Descriptive statistics
> head(summary(hic_imr90_40))
```

```
         seq1 seq2  nbreads nbinteraction averagefreq medfreq sparsity
chr1chr1 chr1 chr1 25914788       4524734      5.7274       1   0.8835
chr2chr1 chr2 chr1   504332        497291      1.0142       1   0.9869
chr3chr1 chr3 chr1   440865        434917      1.0137       1   0.9859
chr4chr1 chr4 chr1   456924        450005      1.0154       1   0.9849
chr5chr1 chr5 chr1   399067        393926      1.0131       1    0.986
chr6chr1 chr6 chr1   382580        377654       1.013       1   0.9858
```

3 Topological Domains

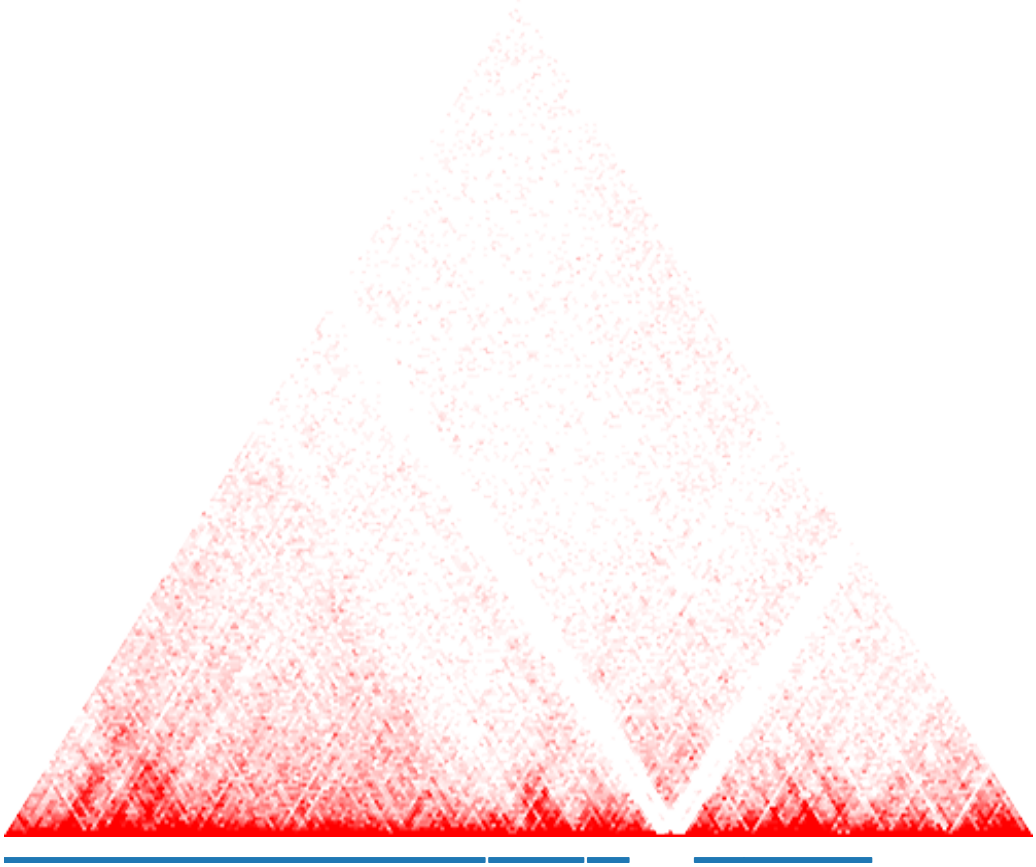
The tads_imr90 object is a *GRanges* object with a all TADs detected from this Hi-C data.

```
> show(tads_imr90)
```

```
GRanges object with 2338 ranges and 0 metadata columns:
          seqnames                ranges strand
             <Rle>             <IRanges>  <Rle>
     TAD-1     chr1     [ 770138, 1290137]      *
     TAD-2     chr1     [1290138, 1850140]      *
     TAD-3     chr1     [1850141, 2330140]      *
     TAD-4     chr1     [2330141, 3610140]      *
     TAD-5     chr1     [3770141, 6077413]      *
       ...      ...                    ...    ...
```

```
  TAD-2334     chrX [146992309, 148552096]      *
  TAD-2335     chrX [148592096, 149929342]      *
  TAD-2336     chrX [149929343, 151969344]      *
  TAD-2337     chrX [152089345, 152746806]      *
  TAD-2338     chrX [152786807, 154946806]      *
  -------
  seqinfo: 23 sequences from an unspecified genome; no seqlengths
```

```
> ## Extract region
> regx <- extractRegion(hic_imr90_40$chrXchrX,
+                       chr="chrX", from=95000000, to=105000000)
> ## Plot Hi-C data with TADs
> plot(regx, tracks=list(tads_imr90), maxrange=20)
```



Package versions

This vignette was generated using the following package versions:

- R version 3.1.2 (2014-10-31), `x86_64-apple-darwin10.8.0`
- Base packages: base, datasets, graphics, grDevices, methods, parallel, stats, stats4, utils
- Other packages: BiocGenerics 0.12.1, GenomeInfoDb 1.2.3, GenomicRanges 1.18.3, HiCDataHumanIMR90 1.0.0, HiTC 1.10.0, IRanges 2.0.0, S4Vectors 0.4.0, XVector 0.6.0
- Loaded via a namespace (and not attached): base64enc 0.1-2, BatchJobs 1.5, BBmisc 1.8, BiocParallel 1.0.0, BiocStyle 1.4.1, Biostrings 2.34.0, bitops 1.0-6, brew 1.0-6, checkmate 1.5.0, codetools 0.2-9, DBI 0.3.1, digest 0.6.4, fail 1.2, foreach 1.4.2, GenomicAlignments 1.2.1, grid 3.1.2, iterators 1.0.7, lattice 0.20-29, Matrix 1.1-4, RColorBrewer 1.0-5, RCurl 1.95-4.4, Rsamtools 1.18.2, RSQLite 1.0.0, rtracklayer 1.26.2, sendmailR 1.2-1, stringr 0.6.2, tools 3.1.2, XML 3.98-1.1, zlibbioc 1.12.0

References

J. R. Dixon, S. Selvaraj, F. Yue, A. Kim, Y. Li, Y. Shen, M. Hu, J. S. Liu, and B. Ren. Topological domains in mammalian genomes identified by analysis of chromatin interactions. *Nature*, Apr 2012. doi: 10.1038/nature11082. URL http://dx.doi.org/10.1038/nature11082.

E. Lieberman-Aiden, N. L. van Berkum, L. Williams, M. Imakaev, T. Ragoczy, A. Telling, I. Amit, B. R. Lajoie, P. J. Sabo, M. O. Dorschner, R. Sandstrom, B. Bernstein, M. A. Bender, M. Groudine, A. Gnirke, J. Stamatoyannopoulos, L. A. Mirny, E. S. Lander, and J. Dekker. Comprehensive mapping of long-range interactions reveals folding principles of the human genome. *Science*, 326(5950):289–293, Oct 2009. doi: 10.1126/science.1181369. URL http://dx.doi.org/10.1126/science.1181369.

E. P. Nora, B. R. Lajoie, E. G. Schulz, L. Giorgetti, I. Okamoto, N. Servant, T. Piolot, N. L. van Berkum, J. Meisig, J. Sedat, J. Gribnau, E. Barillot, N. Bluthgen, J. Dekker, and E. Heard. Spatial partitioning of the regulatory landscape of the x-inactivation centre. *Nature*, Apr 2012. doi: 10.1038/nature11049. URL http://dx.doi.org/10.1038/nature11049.

N. Servant, B. R. Lajoie, E. P. Nora, L. Giorgetti, C. Chen, E. Heard, J. Dekker, and E. Barillot. Hitc : Exploration of high-throughput 'c' experiments. *Bioinformatics*, Aug 2012. doi: 10.1093/bioinformatics/bts521. URL http://dx.doi.org/10.1093/bioinformatics/bts521.