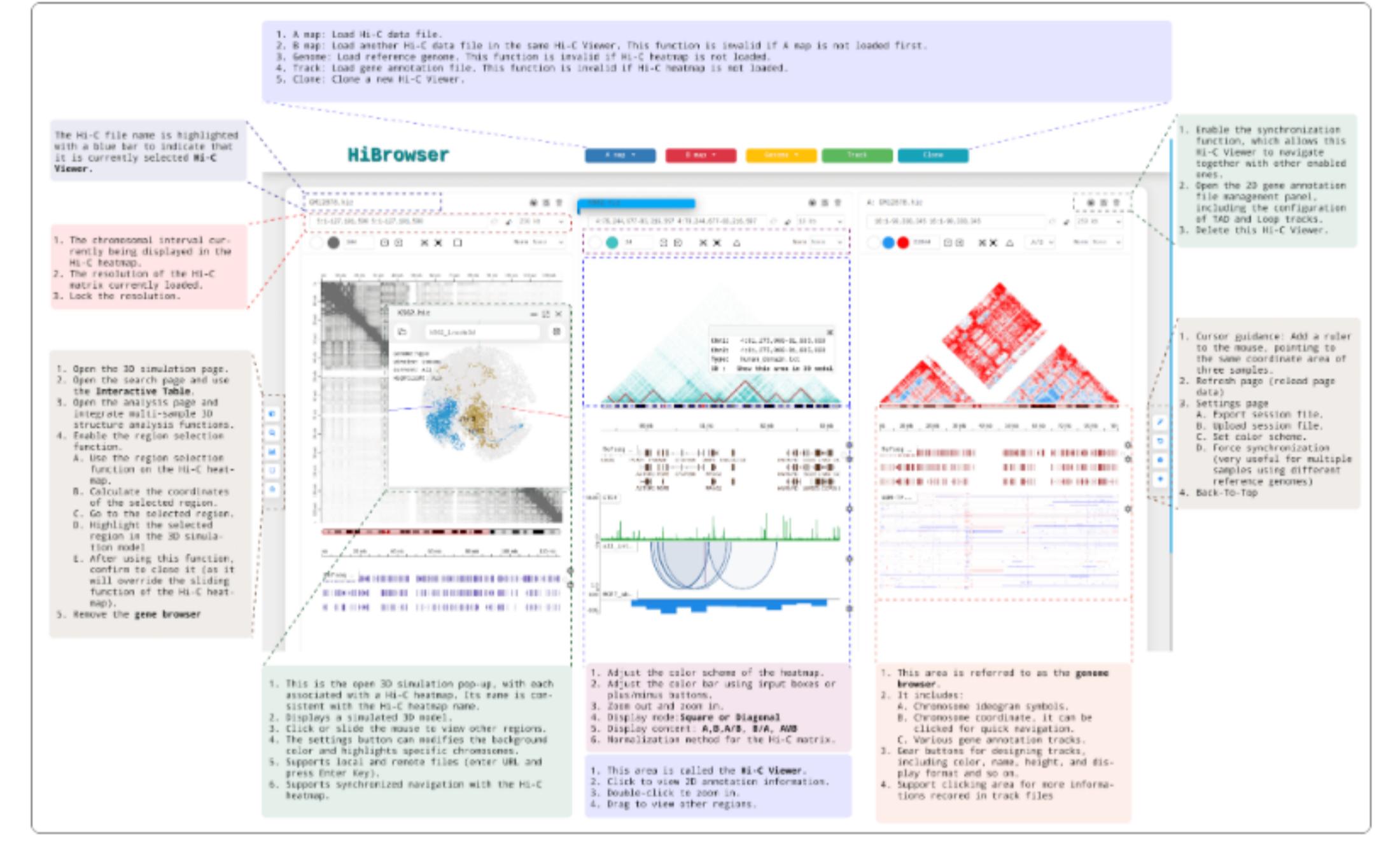


Quick start

Guide to the UI

Example



This screenshot illustrates default Hi-C Map and tracks after adjusting track order and heights to display heat maps.

The interface consists of four main components:

- Header
 - Load Hi-C Map: Button A&B Map
 - Load Gene Browser: Button Genome
 - Load Track
 - Clone
- Hi-C Viewer
 - panel
 - main canvas
- Gene Browser
- Widgets
 - 3D model
 - Search
 - Analyse
 - Others

When entering the app homepage, we will load two(or three, adapt to the display page automatically.) empty Hi-C Viewer by default and use a **blue bar** to indicate the currently selected viewer.

Please pay attention to the Hi-C Viewer you selected(Just click with your mouse), because this will be the key associated with subsequent Gene Browsers and the right widgets(tools).

The following describes the usage of each component in detail.

Load Hi-C Viewer

A map

By clicking this button, you can load a Hi-C file and visualize it.

- Only support .hic file(We will automatically check the files you upload)
- support local file and remote url
- It will be displayed on the viewer you selected
- It will overwrite the previous one, if you have already loaded it

How to use

1. Select one viewer by clicking it if you have cloned 2 or more viewers.
2. Click A map button.
3. If using a remote file, select `remote url` and enter the url which is ended with `.hic`

B map

The button will be disabled if A map is not loaded.

The first .hic file is called **contact map** and the second one called **control map** if they are both loaded into the same Hi-C Viewer.

This function is implemented to compare the differences between samples more conveniently which is supported by juicer box.

By clicking this button, you can load a control Hi-C file and visualize it.

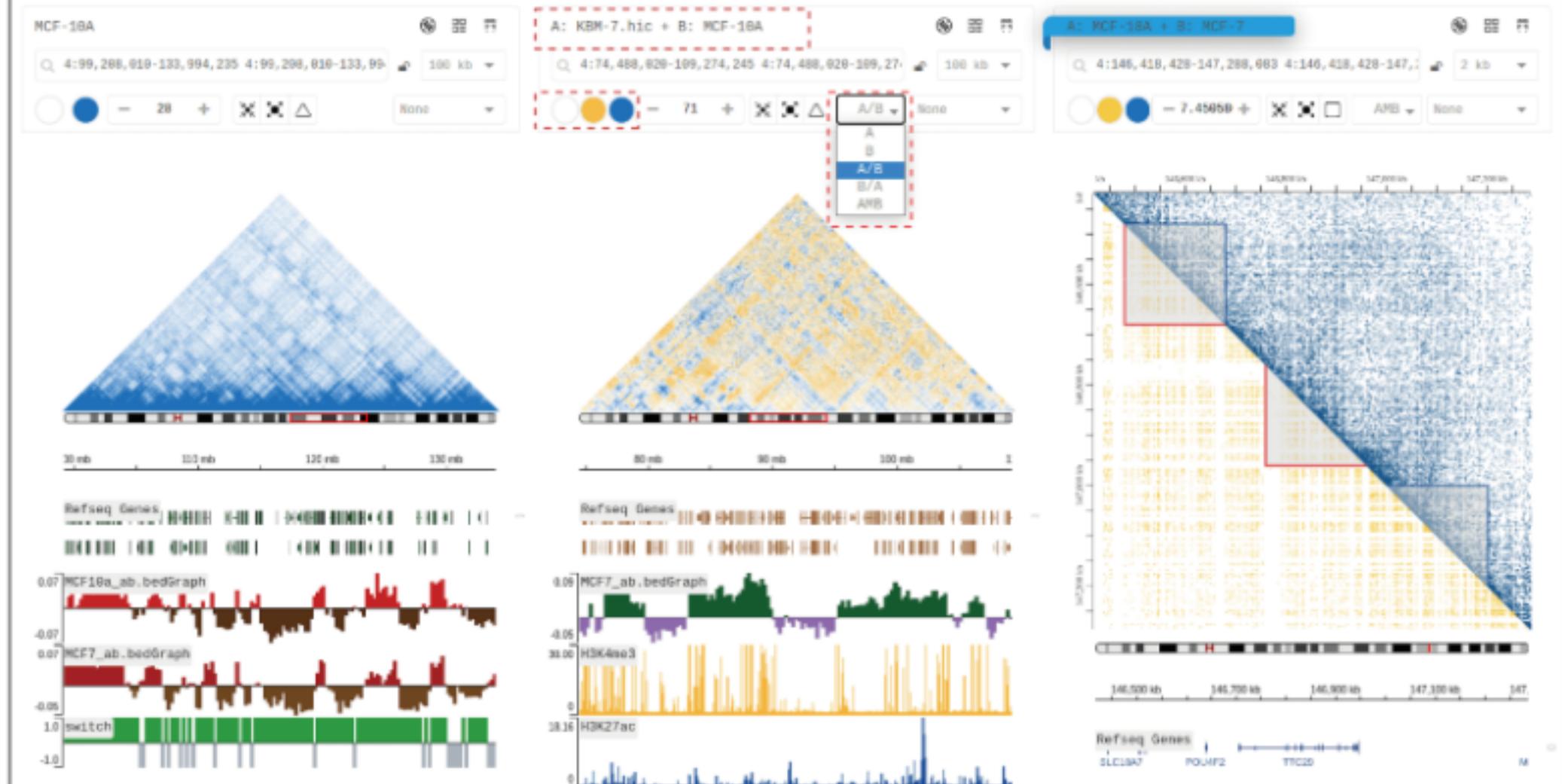
- Only support .hic file(We will automatically check the files you upload)
- Only when you load the contact map will it take effect(Loaded it By clicking Button A map)
- support local file and remote url
- It will overwrite the previous one, if you have already loaded it

How to use

1. Select one viewer by clicking it if you have cloned 2 or more viewers and make sure you have loaded contact map.
2. Click B map button.
3. If using a remote file, select `remote url` and enter the url which is ended with `.hic`

If you are prompted that loading fails, you can confirm whether you have selected the correct viewer.

Example



left:load contact map; middle: load control map; right: change displayed heatmap

Load Gene Browser

By clicking this button, you can load a Gene Browser and visualize it.

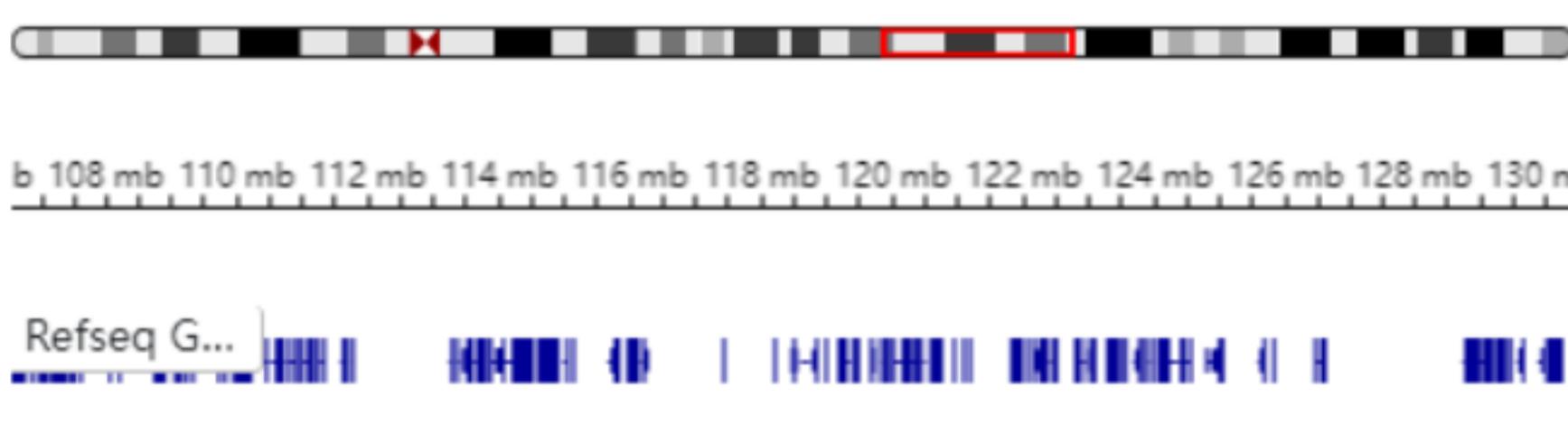
- It requires three files and one optional file. [More details.](#)
 - the reference Genome sequence(.fasta, .fa)
 - the index file of reference Genome sequence(.fai)
 - the refGene(.txt.gz)
 - (*Optional*)the cytoBandIdeo(.txt)
- Only when you load the contact map will it take effect(Loaded it By clicking Button A map)
- It will overwrite the previous one, if you have already loaded it
- support local file and remote url

How to use

1. Select one viewer by clicking it if you have cloned 2 or more viewers and make sure you have loaded contact map.
2. Click `Genome` button.
3. If using remote files, select `remote url` and enter three required urls and one optional url.
4. If using local files, press and hold the keyboard `CTRL`(`command` in Mac), and select three required files and one optional file.

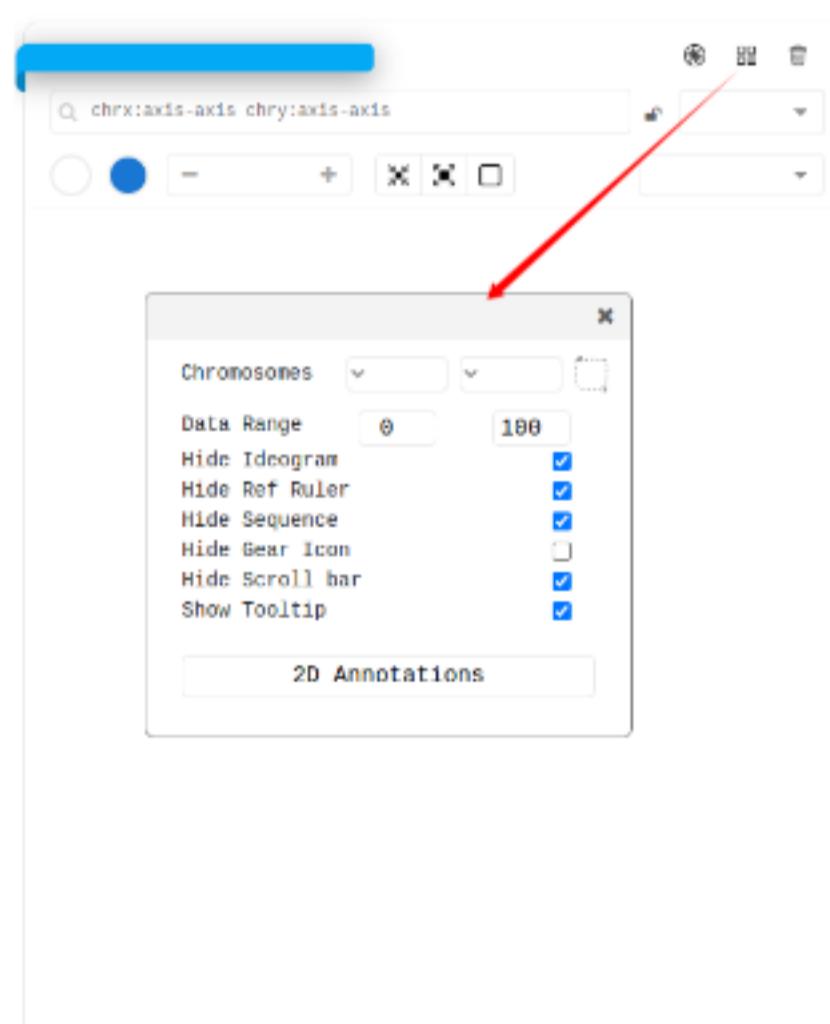
If you are prompted that loading fails, you can confirm whether you have selected the correct viewer.

Example



You can choose whether to display chromosome ideogram, chromosome coordinate axes, chromosome sequences, settings button, and scrollbar. All settings can be changed at any time during runtime.

Example



Load Track

We support displaying 2D annotations on Hi-C Viewer and gene annotations on Gene Browser. [More details.](#)

- support local file and remote url
- support for various file types

How to use

1. Select one viewer by clicking it if you have cloned 2 or more viewers and make sure you have loaded contact map and Gene Browser.
2. Click `track` button.
3. select your track type. [If there is no track type for you, please select `Automactic speculation` (The last one)]
4. Enter the urls or select local files. Note that the local file has higher priority than url.

Example

1. Choose file type:

Select the track Type

2D annotations(supported by Juicebox)

- TAD Domains, processed by tabix in .txt format
- Loop, processed by tabix in .txt format
- A/B compartment, processed by tabix in .bedGraph

Other tracks(supported by IGV)

- Non-quantitative genome annotations - bed, gff, gff3, gtf, bedpe, and others
- Quantitative genomic data - wig, bigWig, bedGraph

Track URL

Index URL

Submit

Clone

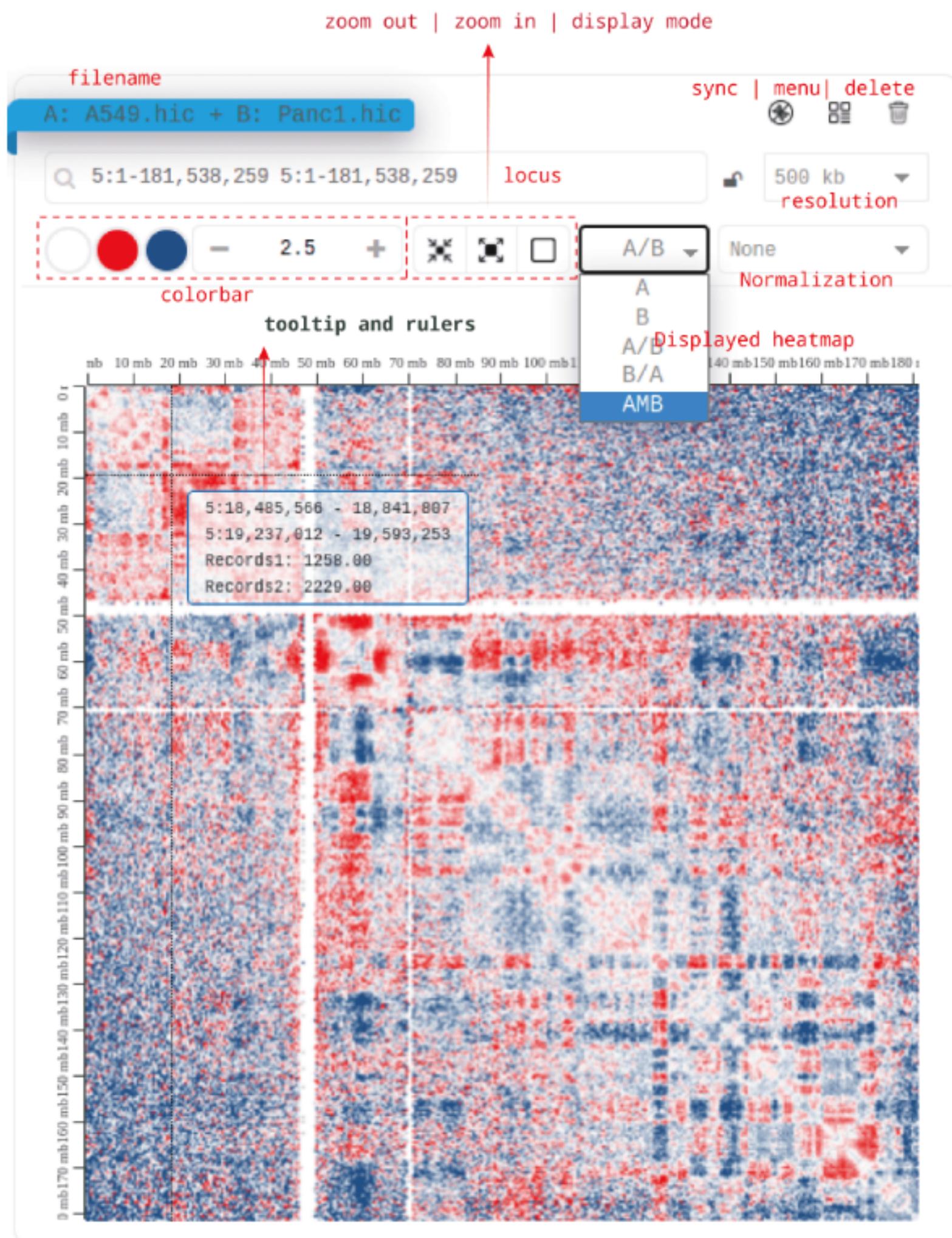
Clone

We take a Hi-C Viewer and a Genome Browser as a whole.

By clicking this button, you can clone this component with empty body.

Hi-C Viewer Panel

Example



filename

file name of contact map. we use the **blue bar**, which is displayed on the file name, to indicate the currently selected browser

Locus

Locate to the chromosome sites quickly(by clicking its right icon)

- Support coordinate : **chrX:start-end chry:start-end(space split)**
 - support omitting prefix `chr` [eg:5:1-181,538,259 5:1-181,538,259]
 - support ommiting chry [eg: 5:1-181,538,259]
 - support ommiting end [eg: 5:1]
- Support gene : gene name

color bar

Set the color bar of the heat map:

- left one: if the value recorded in .hic is equal to min value
- right one: if the value recorded in .hic is equal to max value

If B map is loaded, the colorbar will add to three. At this point:

When both A and B map are loaded simultaneously, the color is calculated by $\log(a/b)$.

- left one: if the value is equal to 0
- middle one: if the value is negative
- right one: if the value is positive

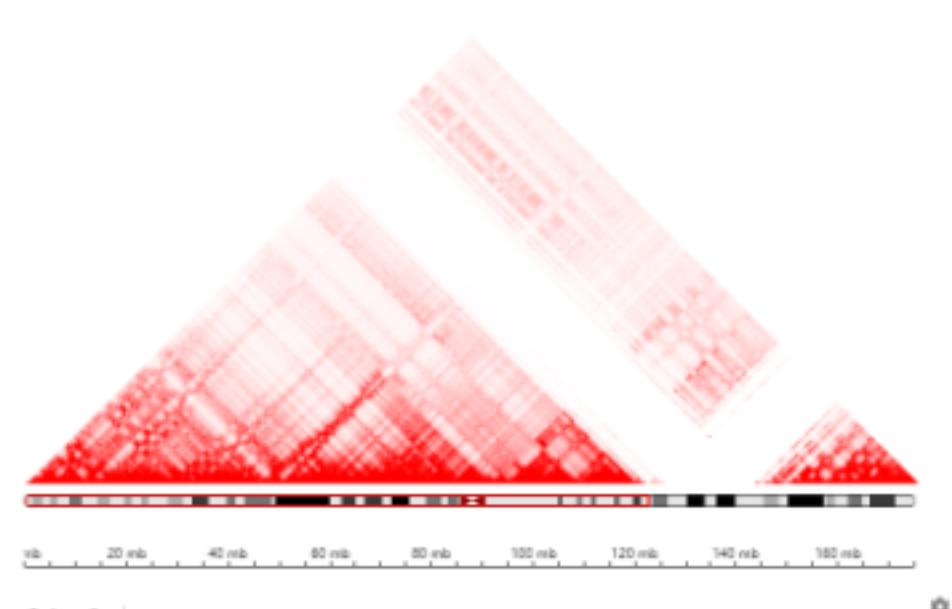
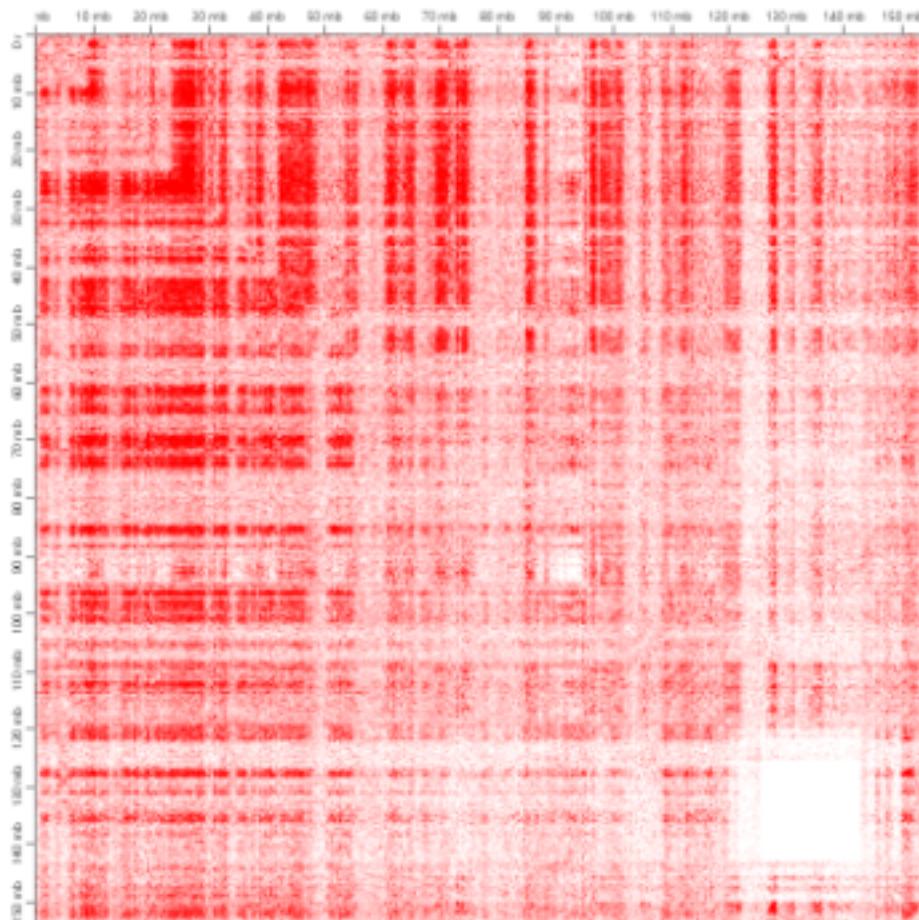
Tooltip and rulers

Display the current record value of loaded Hi-C data at the mouse cursor.

Display mode

- horizontal triangular heatmap
- two-dimensional heatmap

Example



left: inter-contact between chr X and chr Y; right : intra-contact of chr 1

Displayed mode

- A
- B
- A/B
- B/A
- AMB

In the mode od "AMB", the lower-left and upper-right parts of a view display the contact maps of A and B respectively. And 2D annotations associated with two samples (A and B) are displayed in the corresponding lower-left and upper-right of the heatmap

Threshold of contact value

Controls the color depth of the heat map. The higher the value, the lighter the heat map color

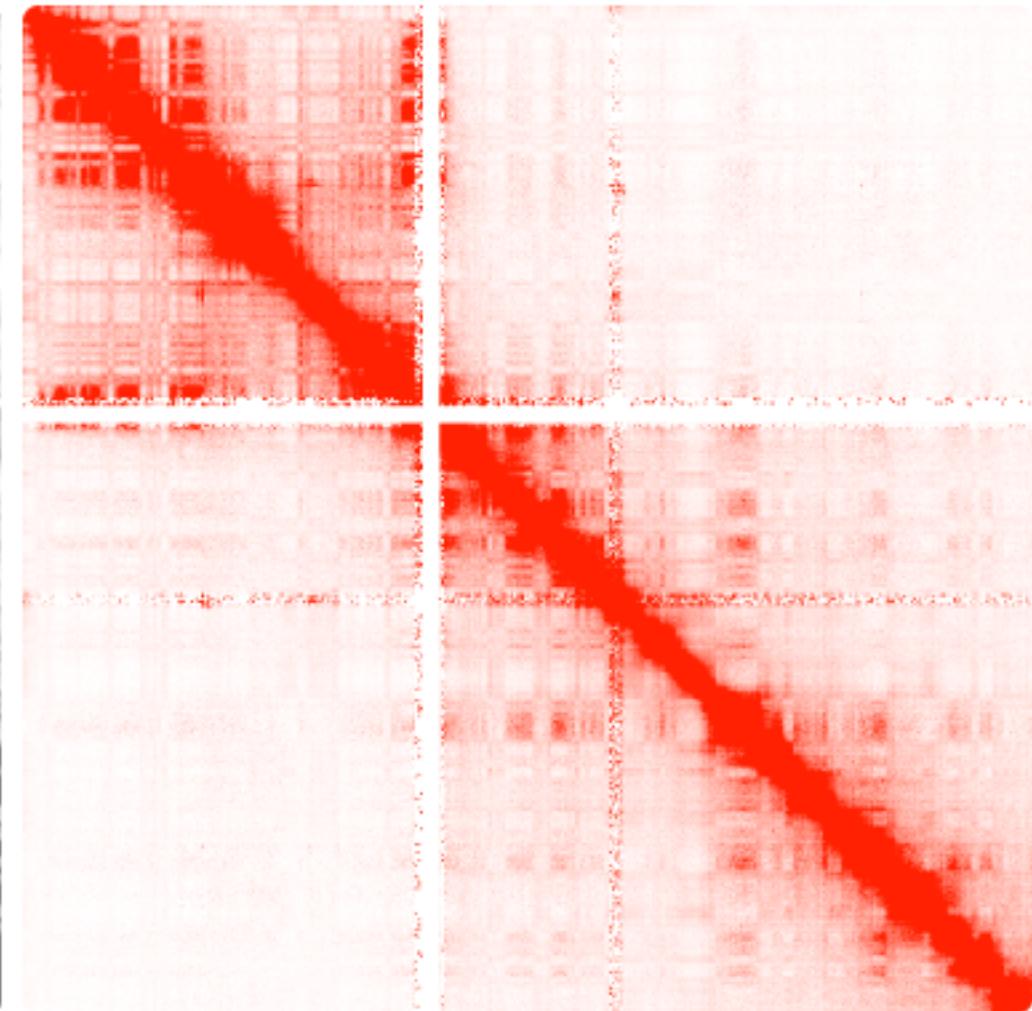
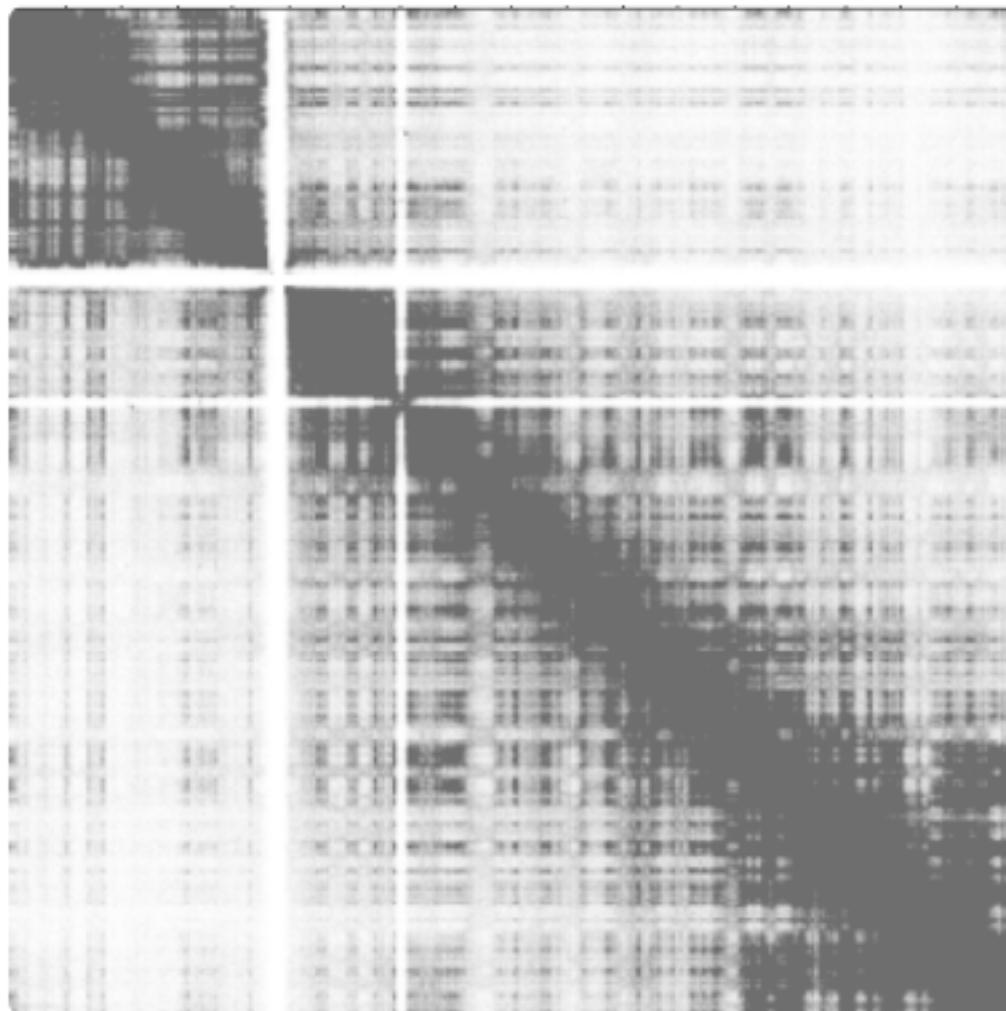
normalization

different normalization of Hi-C contact Matrix

resolution

Adjust the resolution to view more detailed

Example



Adjust color bar and threshold. The resolution and normalization are changed for the right

Zoom in & Zoom out

The functions are the same as their name.

lock

lock the select option resolution

delete

delete this Hi-C Viewer(if there are two or more)

Hi-C Viewer Canvas

X axis and Y axis

By clicking it, the canvas zooms into the intra-chromosome heatmap

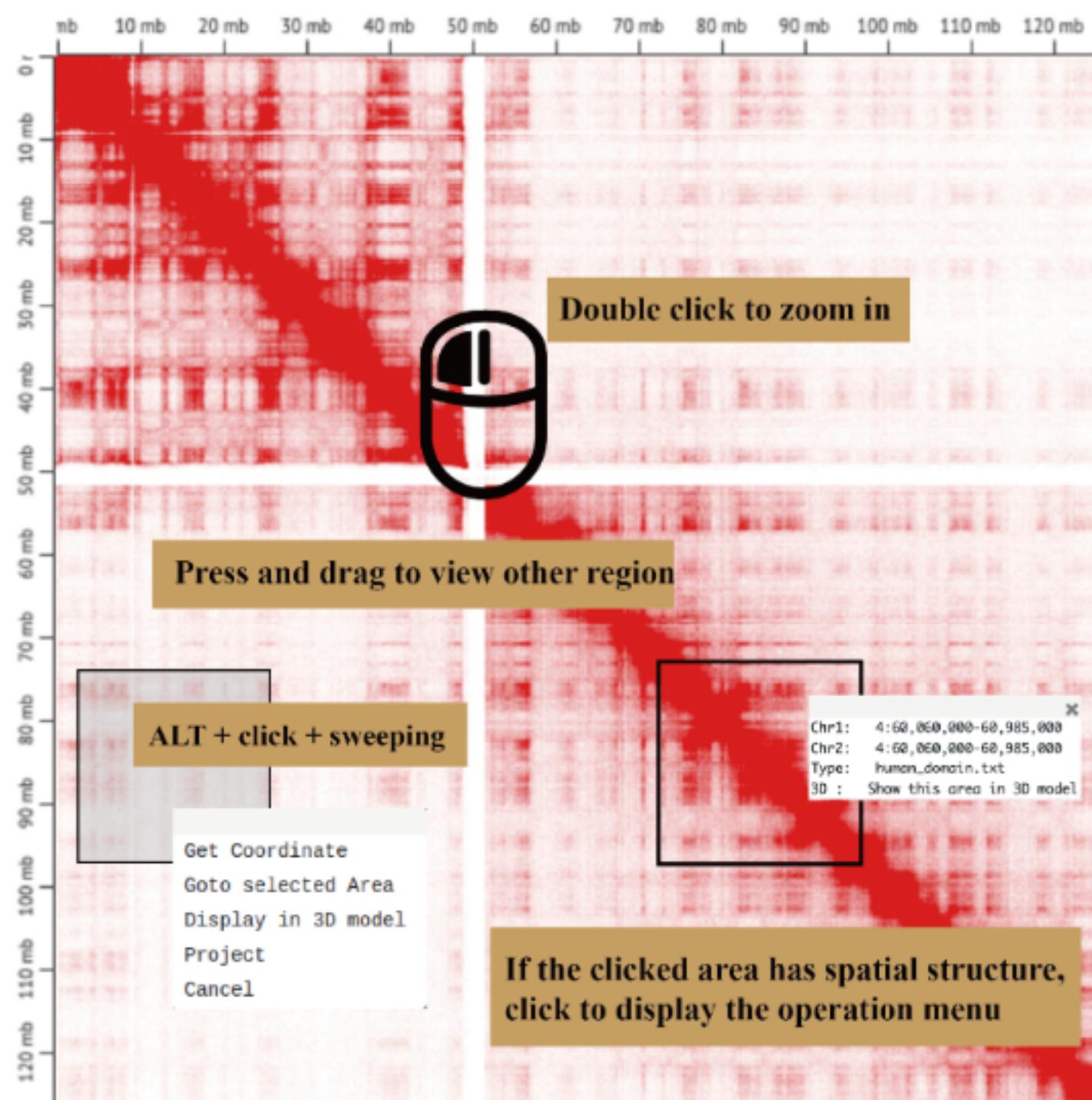
canvas

By double clicking it, the canvas can zoom into more details

By dragging it, you can view heat map of other regions of chromosome

How to use

Example



2d track menu

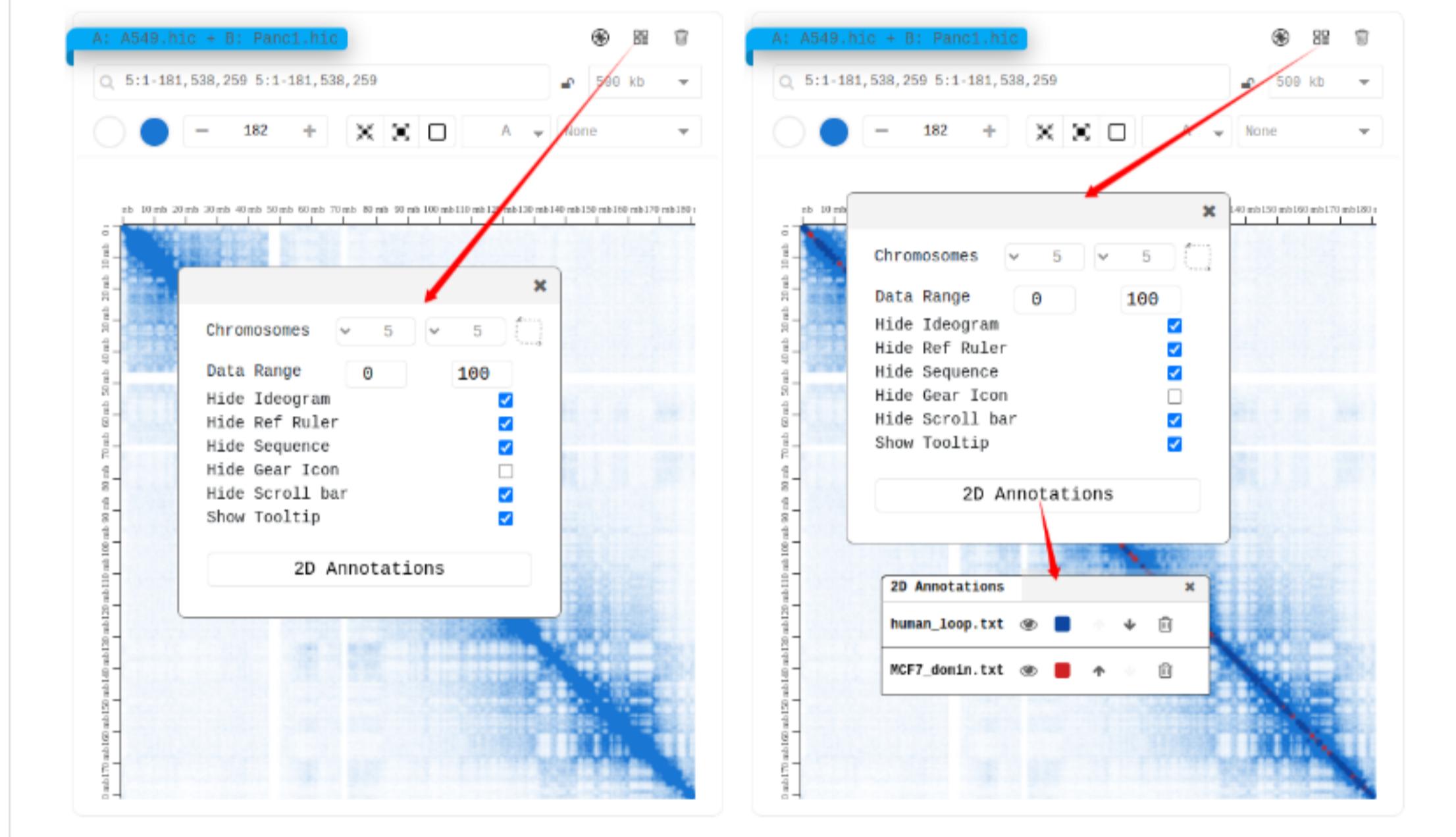
Here, you can quickly locate the whole chromosome.

adjust the heatmap data display range during runtime, (e.g., filtering out low-frequency remote interactions or high-frequency internal interactions)

If you loaded 2d tracks, you can also manage them here, such as adjusting colors, deleting, etc

You can also modify some settings related to the genome browser.

Example



sync

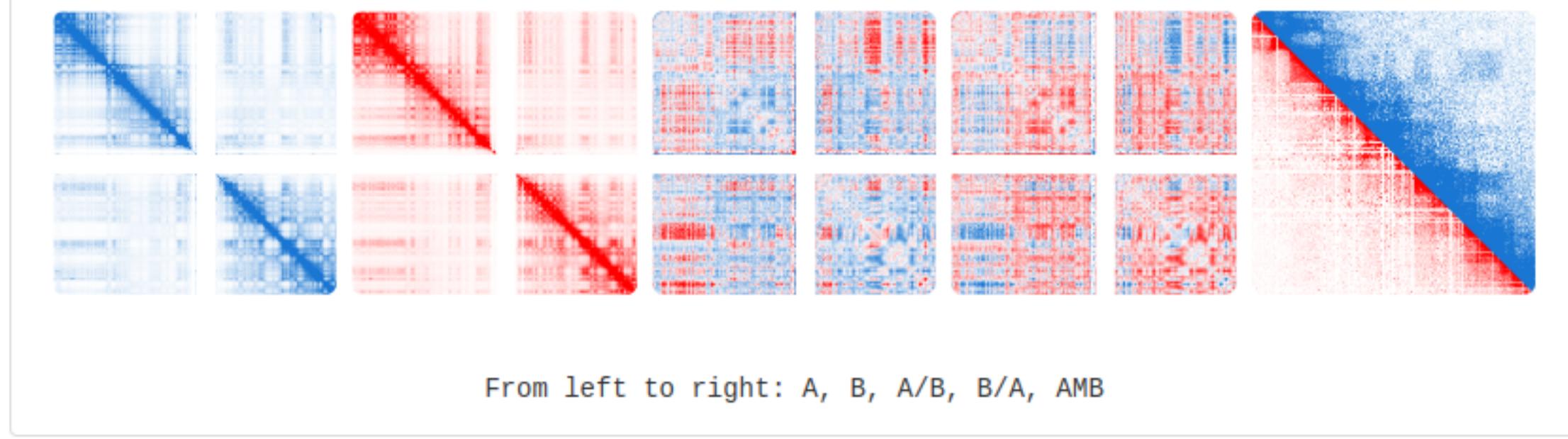
See Next Section.

control map panel

Select the matrix displayed on canvas:

- A:Contact Map
- B:Control Map
- A/B
- B/A

Example



From left to right: A, B, A/B, B/A, AMB

Browser Sync

Multiomics and Sample differences are of great significance to the study of biological gene regulatory network and epigenetic network.

Our browser provides two collaborative visualization functions

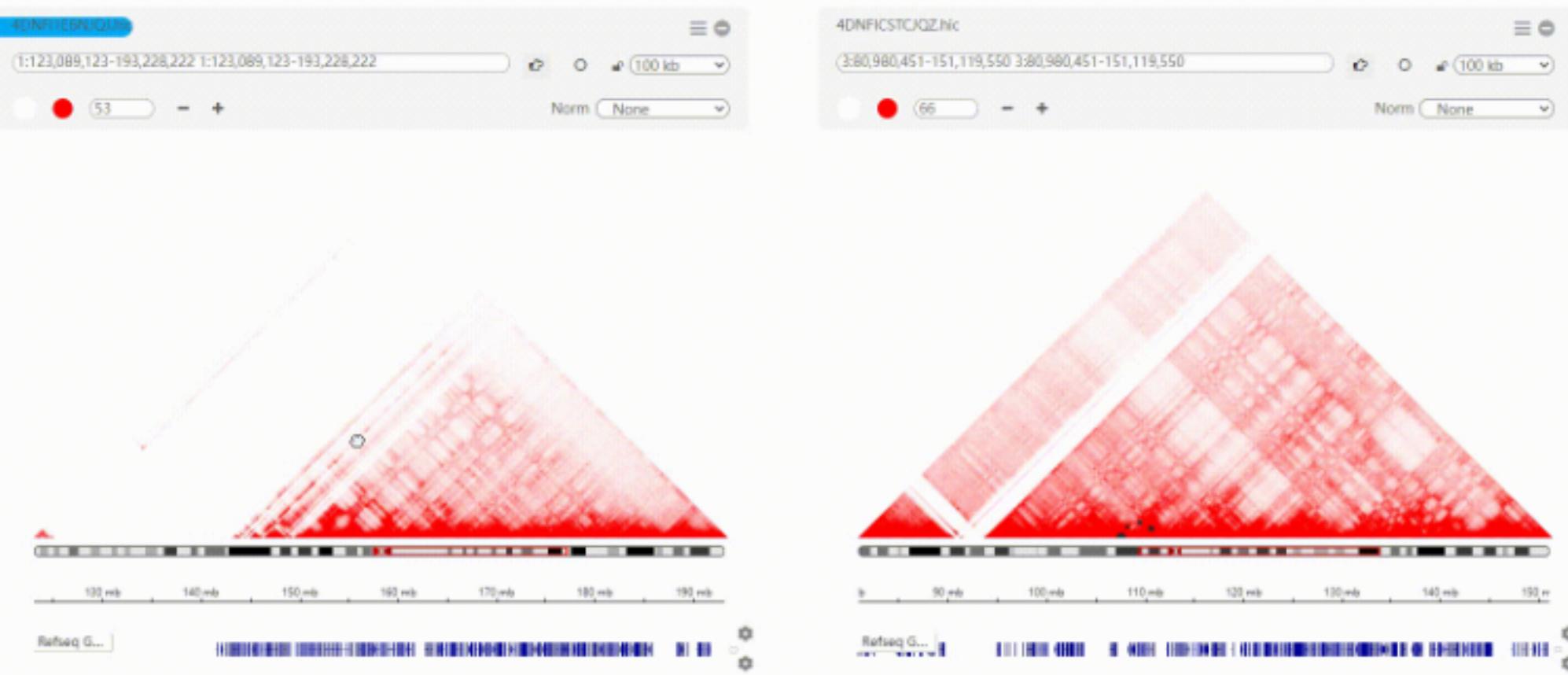
- Synchronization between Hi-C and Gene Browser
- Synchronization between two and more Hi-C and Gene Browser

After loading the Gene browser, it will synchronize with its associated hic browser.

That is, if you drag or zoom in or out the Hi-C Viewer, the Gene Browser will also synchronize, and vice versa.

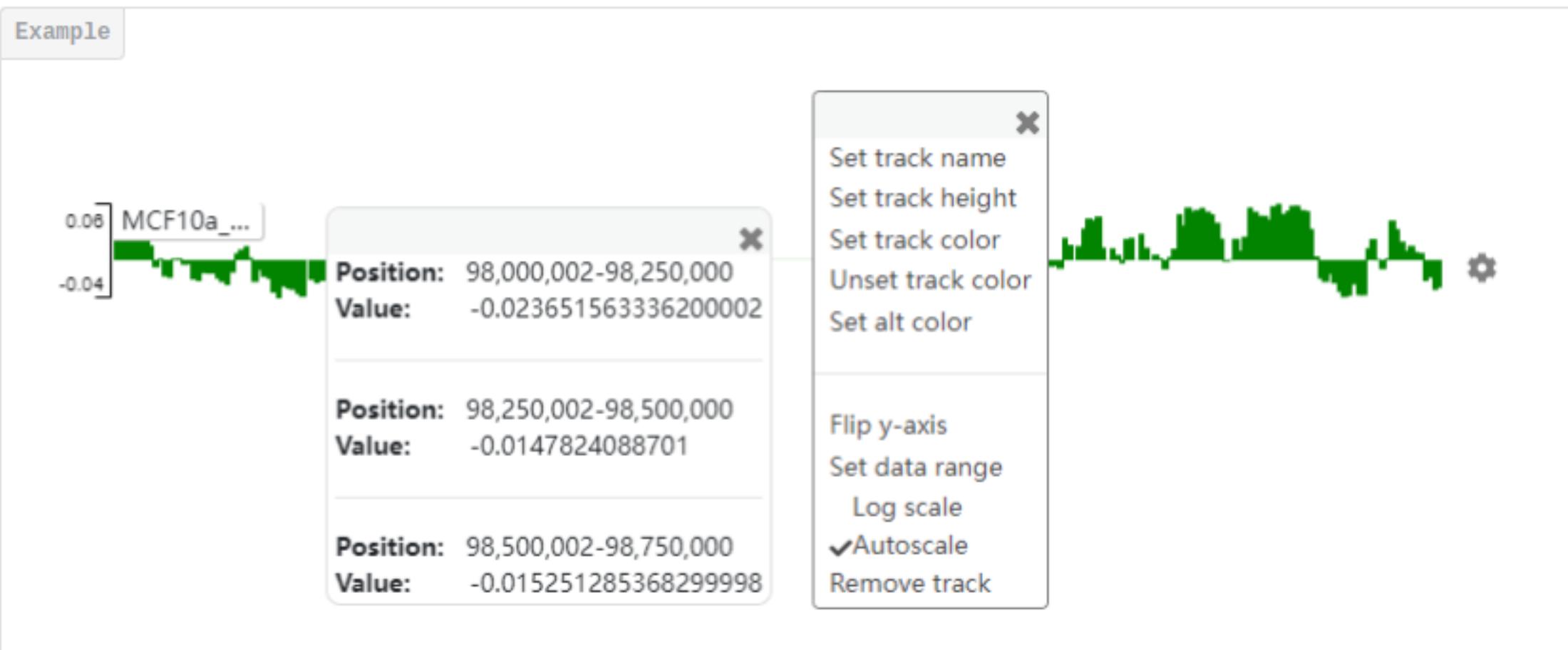
In addition, we provide a *sync button* on the Hi-C panel to synchronize multiple samples by clicking it.

Example



Genome Browser

We embed igv as our Gene Browser and integrated their functions as result.



By clicking the gear icon, you can modify the property of loaded track.

By clicking the canvas, you can view more detail infos record in your track files.

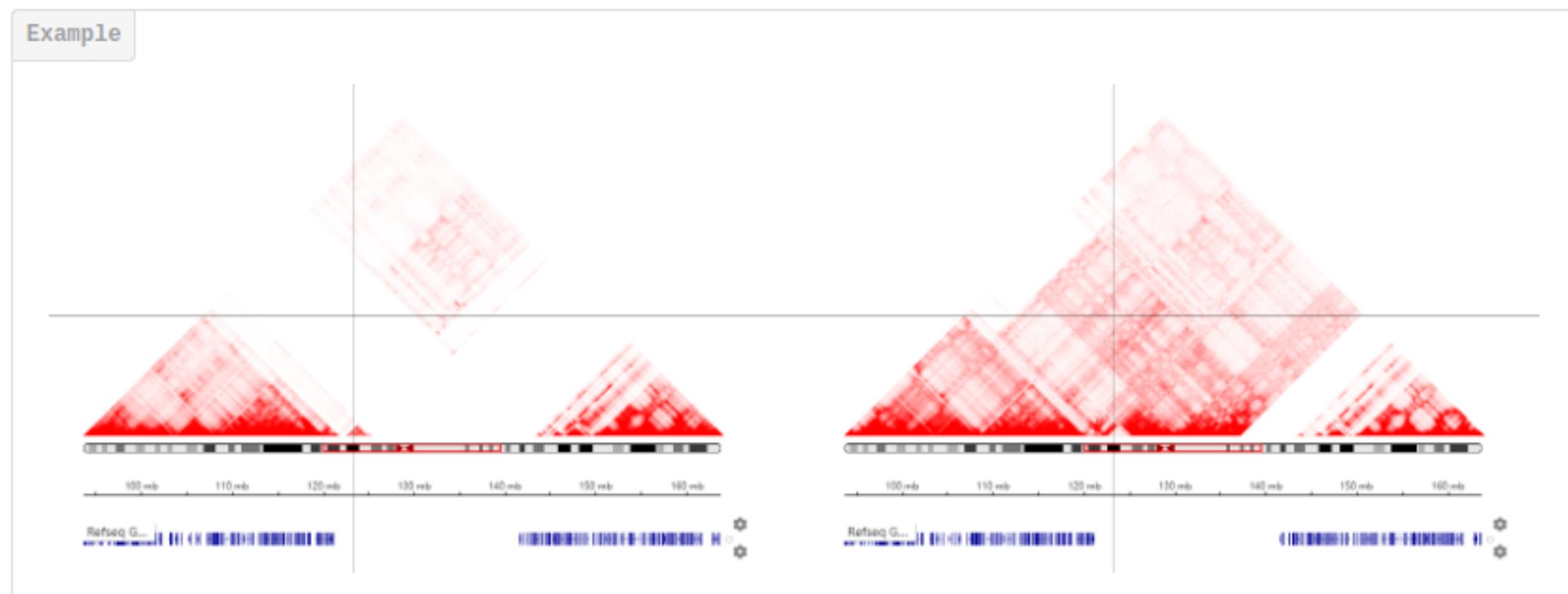
Widgets

To explore more information in the hic heatmap, we provide very rich expansion components.

3D model

see in [here](#)

Cursour guide



Add guide line at your mouse pointer, and locate the same site on different samples

Search

see in [here](#)

Analyse

see in [here](#)

Refresh

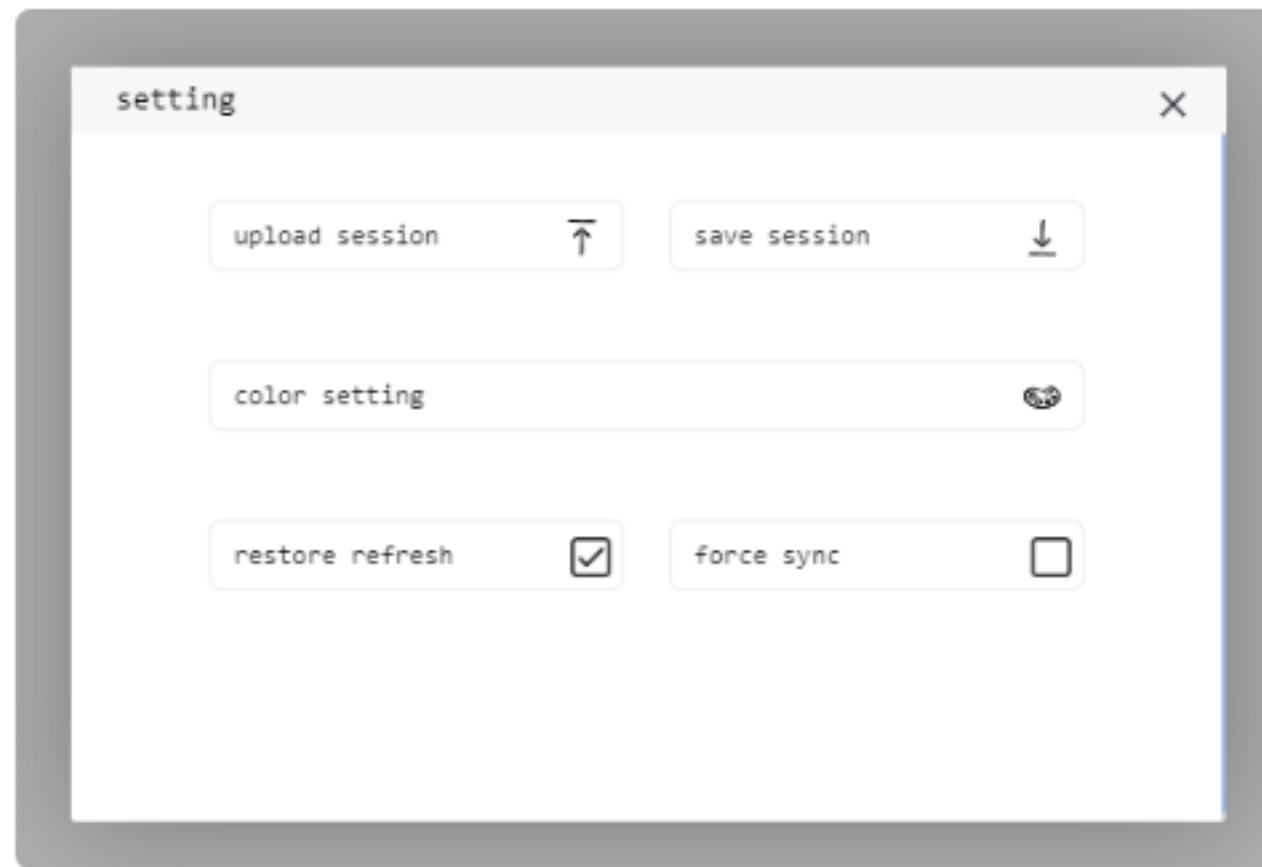
We suggest using this widget to refresh the page instead of using 'F5' or the reload button of your browser. Because this widget will save the current session of the browser which is vatal for restoring. See **Setting** below.

Using F5 or others, our browser can not read the latest session. It may load a session that saved a long time ago.

Setting

Personal setting

Example



Save Session

Save current browser statuses, including various loaded data.

For security reasons, the browser cannot actively access your device data, so the data loaded locally cannot be saved.

upload Session

Upload a session file, and restore to a consistent state.

Restore while Refresh

Restore a consistent state, while you refresh the browser page.

For security reasons, the browser cannot actively access your device data, so the data loaded locally cannot be restored.

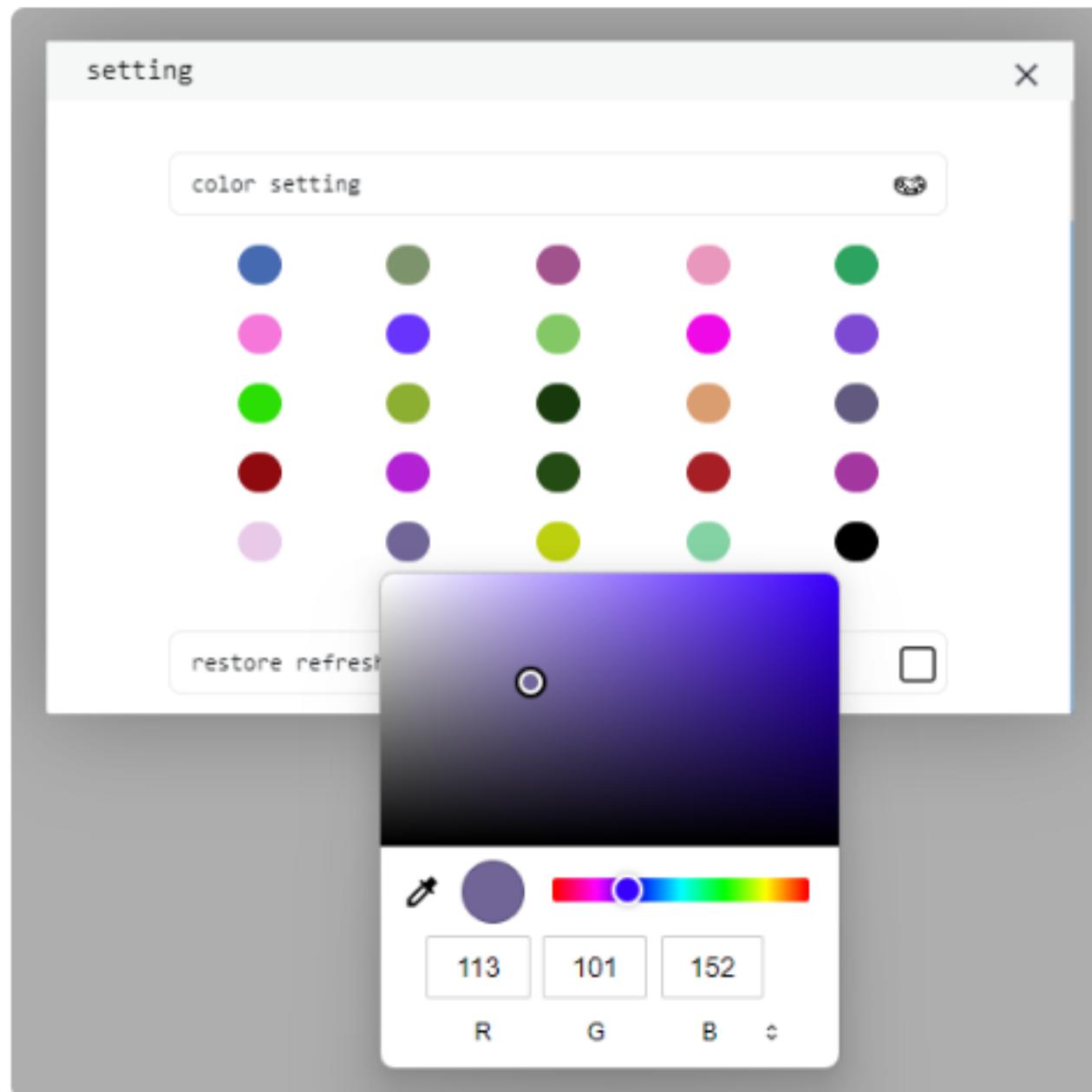
Force Sync

see [here](#).

When different reference genes are used, they will not be synchronized. You can force to be synchronized, which is very useful when studying different species.

Color setting

Example

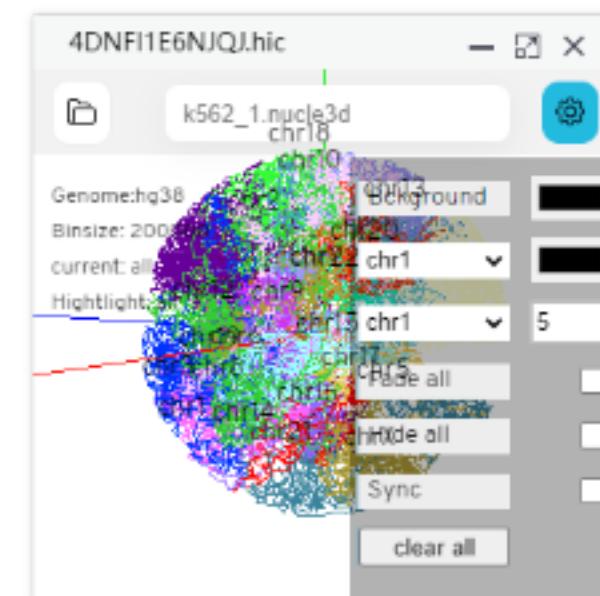
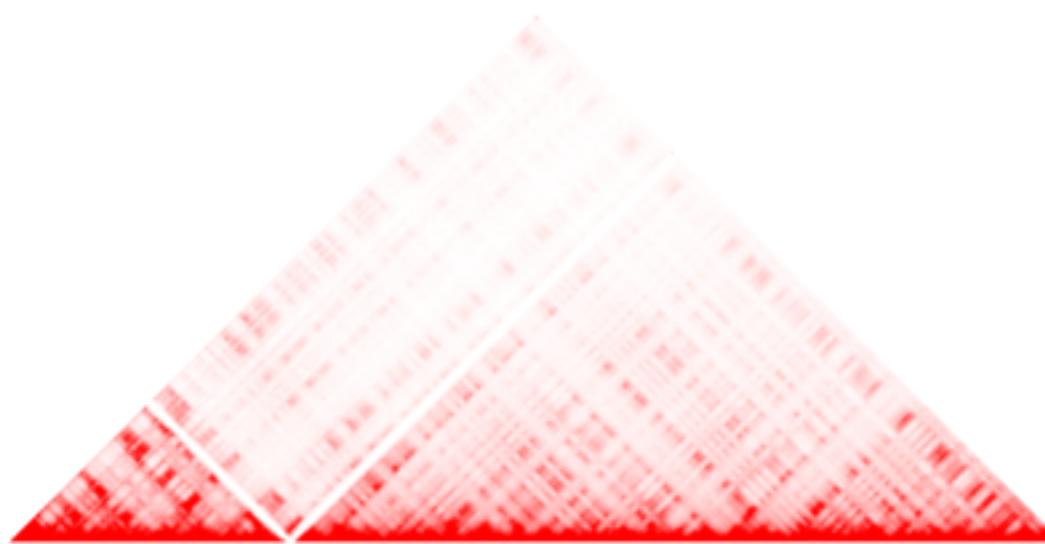


default colors

Provide color groups for [analyze page](#), We will give priority to the colors you provide.

3D model

Example



In order to understand the 3d structure of genes, for example teaching, we provide a 3d visualization function.

You must load the Hi-C file to use this extended function, or you can go to a separate page we provided.

3D model panel

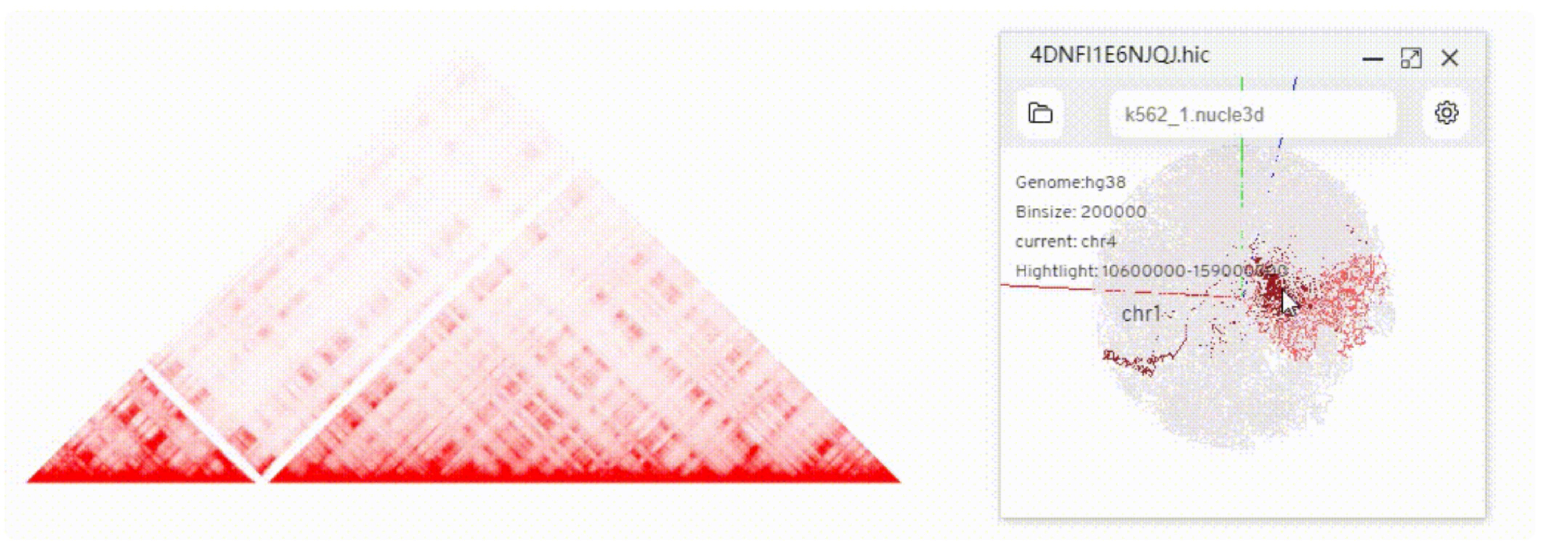
- file icon : upload your local 3d track(for more, see [here](#))
- input file : show the track file name, also, you can type you remote url and press `enter` in your keyboard to load it.
- setting icon:
 - Modify background color
 - Modify chromosome color
 - Modify chromosome width
 - hide all
 - fade all
 - clear all
 - sync : sync with HiBrowser

Sync with Hic Viewer

When you view the Hi-C heat map, you can see the 3D structure of the segment synchronously and its spatial position with other chromosomes.

This feature may reduce some browser performance, such as fps.

Example



Search

The technological developments of recent years have dramatically accelerated the discovery and characterization of SVs, expanded our knowledge of the 3D nature of chromatin folding and assigned functionality to large parts of the non-coding Genome.¹

In order to study the way of participating in gene regulation over a long distance, we have processed data from many sources, including hic experiment, gene annotation, enhancer annotation, human transcriptional regulatory networks, disease related.

We use interaction table module to display the strongly related data.

You must load the Hi-C file to use this extended function

Example

Locus	APP	Q	APP	Q				
NM_001136131	APP	Q	chr9:119033415-1...	chr14:35015413-3...	-	CTCF(+),ETS2(?),H...		Alzheimer's Disease...
NM_006380	APPBP2	Q			-			
NM_012096	APPL1	Q			+			MATURITY-ONSET...
NM_001251905	APPL2	Q			-			
NM_001306151	DAPP1	Q			+			
NM_018453	EAPP	Q		chr14:35015413-3...	-	EGR1(+),SP1(+),SP...	ABCB1(+),CDKN1A...	
NM_000415	IAPP	Q			+	GATA4(+)		
NR_027131	NKAPP1	Q			-			
NM_002581	PAPPA	Q	chr9:119033415-1...		+			
NR_103711	PAPPA-AS1	Q			-			
NM_020318	PAPPA2	Q			+			
NM_001166621	TRAPPC1	Q			-			
NM_003274	TRAPPC10	Q			+			
NM_021942	TRAPPC11	Q			+			Autosomal recessi...
NM_016030	TRAPPC12	Q			+			ENCEPHALOPATHY...
NM_001365342	TRAPPC13	Q			+			
NM_001128835	TRAPPC2	Q			-			Spondyloepiphyse...
NM_001355204	TRAPPC2B	Q			+			

Here you can choose:

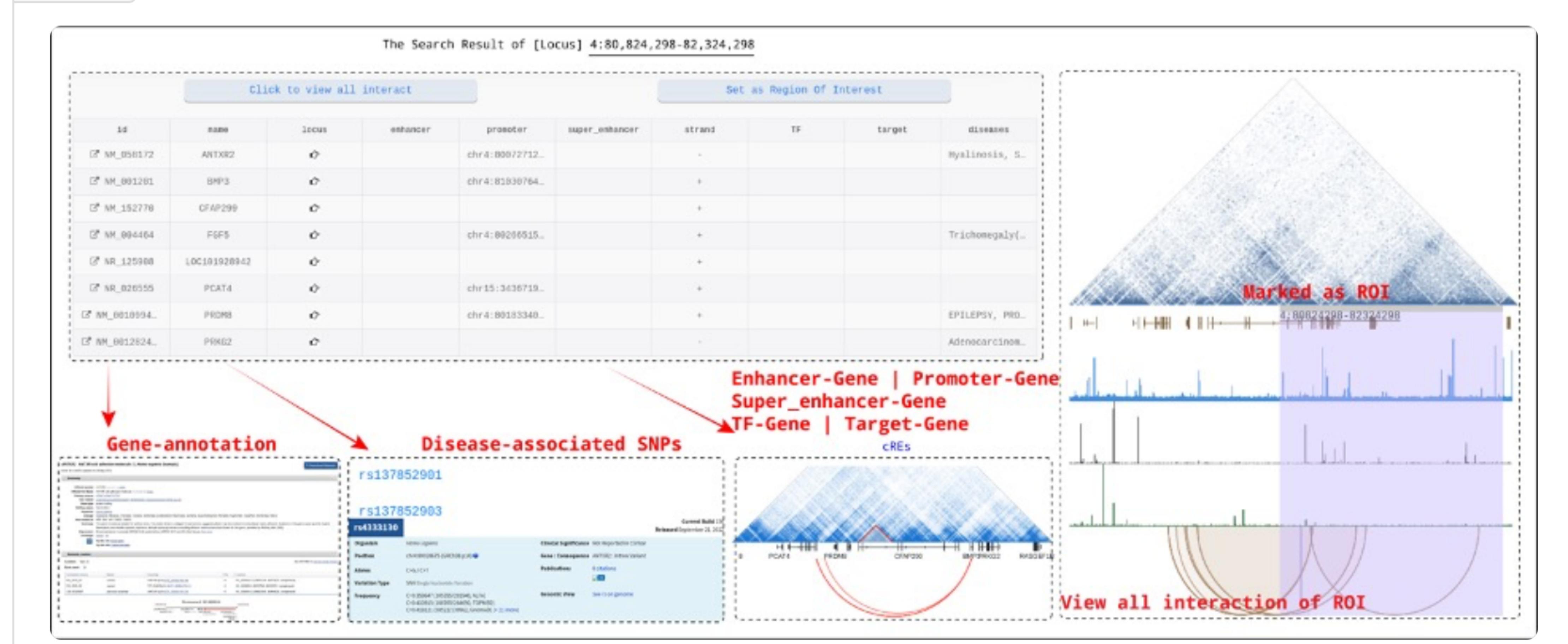
- Gene
- Locus
- Disease

as the keyword for querying.

Example

Locus	APP	Q	APP	Q				
NM_001136131	APP	Q	chr9:119033415-1...	chr14:35015413-3...	-	CTCF(+),ETS2(?),H...		Alzheimer's Disease...
NM_006380	APPBP2	Q			-			
NM_012096	APPL1	Q			+			MATURITY-ONSET...
NM_001251905	APPL2	Q			-			
NM_001306151	DAPP1	Q			+			
NM_018453	EAPP	Q			-			
NM_000415	IAPP	Q			+	GATA4(+)		
NR_027131	NKAPP1	Q			-			
NM_002581	PAPPA	Q	chr9:119033415-1...		+			
NR_103711	PAPPA-AS1	Q			-			
NM_020318	PAPPA2	Q			+			
NM_001166621	TRAPPC1	Q			-			

In each column of the interaction table, you can click to view the details and associate them with the Hi-C Viewer



Analyse

At the chromosome level, Hi-C technology reveals that chromatin can be divided into A/B components, where A is related with accessible and transcriptionally active euchromatin while B is the opposite.

With the increase of sequencing depth(resolution), A/B compartments are subdivided into topological associated domain(TAD). Within TAD, regulatory elements interact with regulated genes.

When the sequencing depth reaches 5kb, the structure of chromatin loop can be detected. The mutation of non coding region often leads to the destruction of loop structure.

In addition to adding TAD, A/B compartment and Loop annotation files on Hi-C Viewer and Genome Browser, we also provide a visual page for basic diversity analysis.

All chart can be exported as svg, picture and pdf.

One sample



The page is divided into three areas:

- Track infos
 - Hi-C file
 - 2D annotations
 - move button
- Track overview
 - the overview of TAD and Loop for the first card
 - the overview of TAD and Loop for the first and second cards
 - the overview of A/B compartment for the first and second cards
- Track details
 - Summary of selected areas
 - Records in your track files
 - Gene annotation respectively

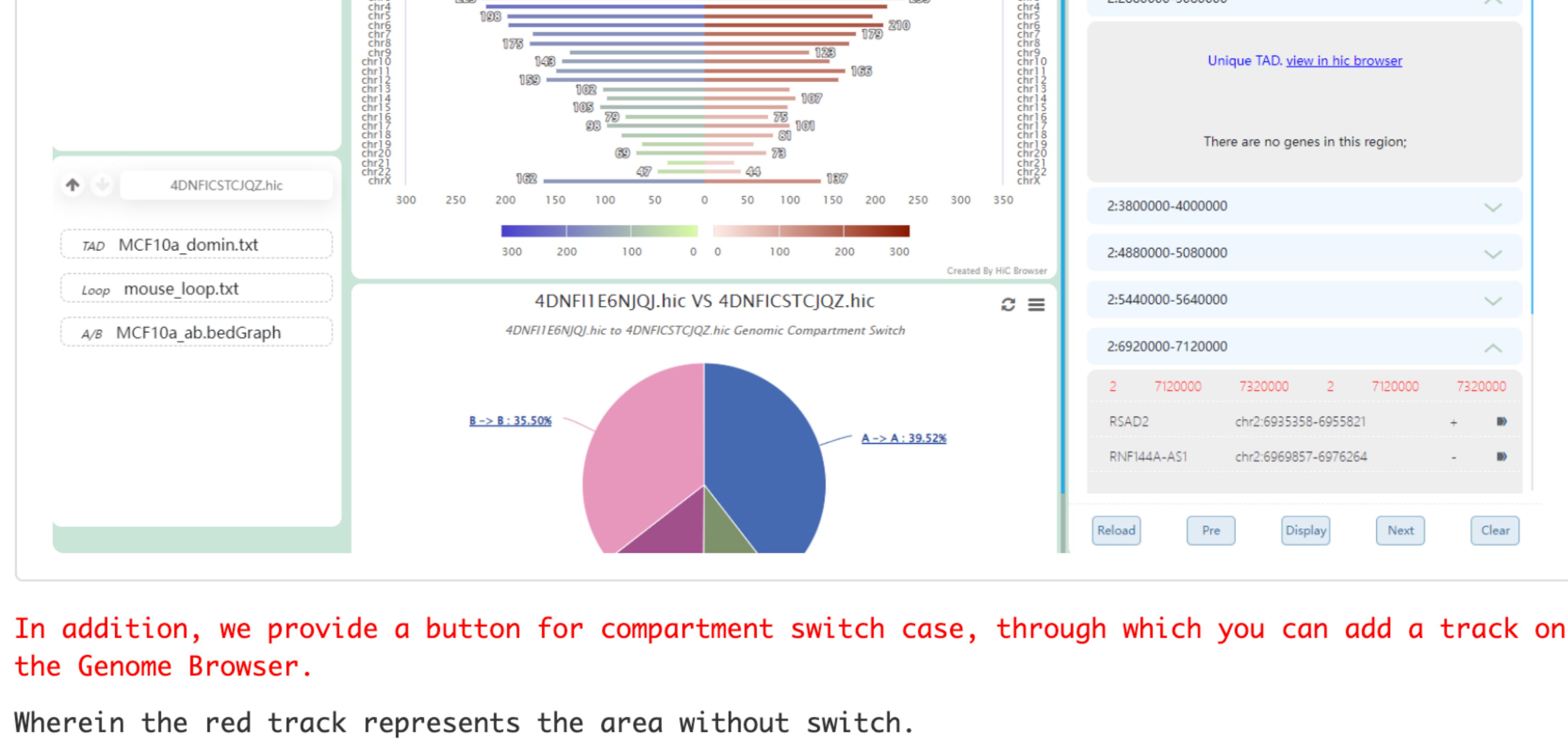
Two and more samples

When two or more samples are loaded, we will show the differences between the first two samples.

Note that in the details area on the right, we use different colors to mark different comparison results:

- Green : Have the same 2D annotation
- Red : Have the changed 2D annotation
- Blue : Sample Unique 2D annotation

You can click the up or down buttons on the left card to adjust the position, so as to modify the samples you want to compare



In addition, we provide a button for compartment switch case, through which you can add a track on the Genome Browser.

Wherein the red track represents the area without switch.



Hi-C Map

In order to use HiBrowser to view three dimensional conformation of chromosome, you need to convert your file into [.hic](#) format.

- We strongly recommend using [juicer pipeline](#) to process your fasta files
- If you have data in other formats such as .cool, [Hi-CExplorer](#) may help you with some format processing
- [Straw](#) is a useful software for reading .hic files

Reference Genome sequence

In order to use the Gene Browser, you need to prepare the reference genome. three required files and one optional file.

- the reference Genome sequence(.fasta, .fa)
- the index file of reference Genome sequence(.fai)
- the refGene(.txt.gz)
- (*Optional*)the cytoBandIdeo(.txt)

Where can we download reference Genome sequence?

- NCBI
- Ensemble
- GENCODE
- UCSC
- <https://hgdownload.soe.ucsc.edu/goldenPath/hg38/bigZips/hg38.fa.gz>
- <https://genomes.yseq.net/WGS/ref/hg38/hg38.fa>
- ...

How can we obtain the index file?

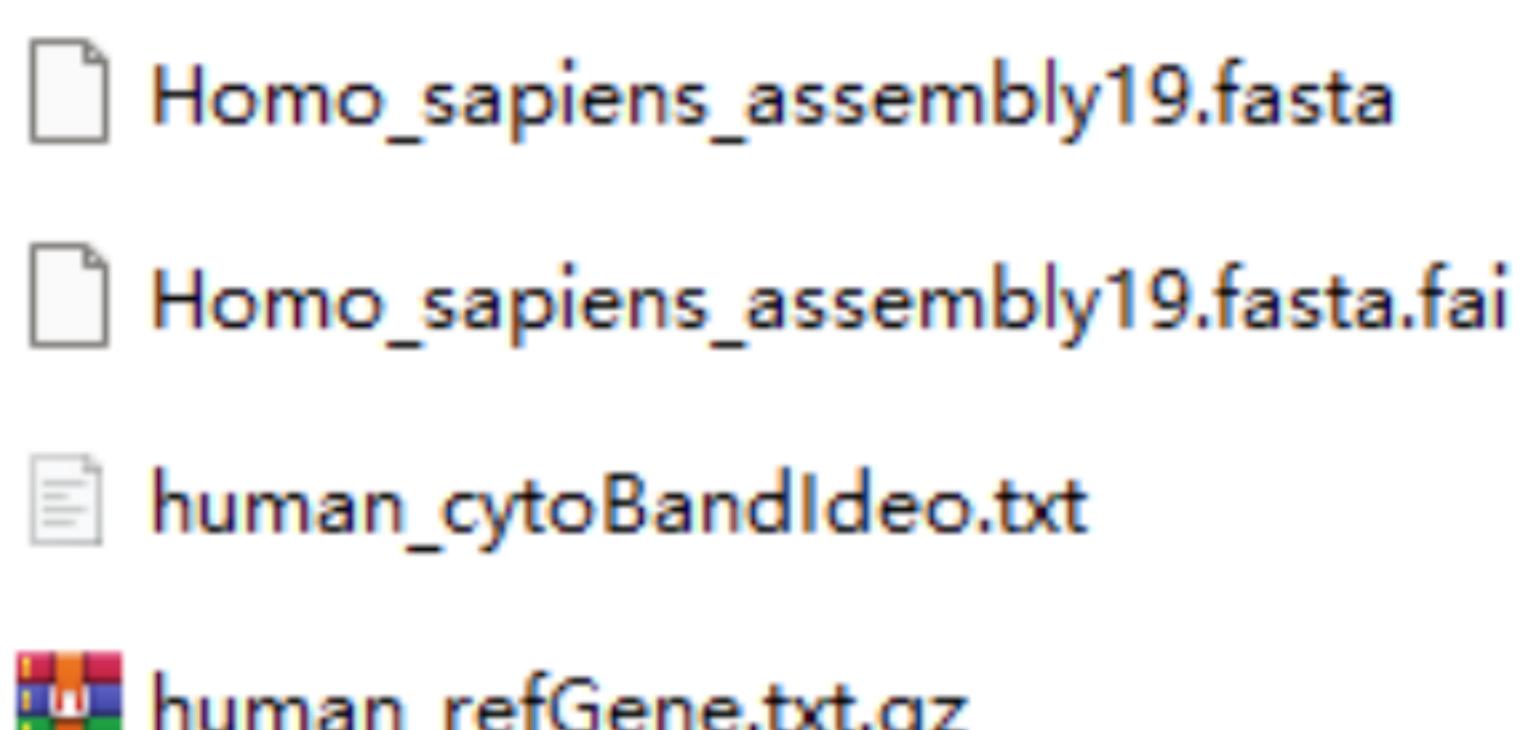
- Install the samtools

```
samtools faidx refGene.fa # *.fa or *.fasta is your input sequence
```

How to download refGene and cytoBandIdeo?

1. Visit [page](#)
2. Select Species
3. Select Version
4. Click Annotations > SQL table dump annotations
5. Search cytoBandIdeo (refGene)
6. Download cytoBandIdeo.txt.gz (refGene.txt.gz)

Example



Our server provides a human reference genome(hg19).

2D Annotation

A/B Compartment, TAD and Loop are three very important three-dimensional structures that identified from interaction matrix.

To distinguish them from gene annotations, we call it 2D Annotation.

TAD and Loop file format(.txt file)

- chr1 : chr1 or 1 (We recommend using 1 instead of chr1)
- x1 : start point
- x2 : end point
- chr2 : same as col chr1 for TAD
- y1 : same as col x1 for TAD
- y2 : same as col x2 for TAD
- color : (optional) a rbg color

In addition to the above six columns, you can add anything later.

[Below is a sample of TAD file \(tab-delimited\)](#) or you can [download it](#).

1	4835000	5835000	1	4835000	5835000	255,255,0	0.5	0.3	0.2	0.4	0.5
X	3360000	4895000	1	3360000	4895000	255,255,0	1.1	0.2	0.2	0.7	0.6

A/B compartment file format(.bedGraph file)

We use gene browser to show A/B compartment

- chr : chr1 or 1 (We recommend using 1 instead of chr1)
- start : start point
- end : end point
- eigen1 : eigenvalue of first principal component

In addition to the above 4 columns, you can add anything later, such as eigen2, eigen3 ... All information can be displayed in the browser.

[Below is a sample of A/B compartment file \(tab-delimited\)](#) or you can [download it](#).

chr1	500001	750000	0.0139276847711	-0.00805369000596	0.0031572649846700004
chr1	750001	1000000	0.0597001694219	0.00840457775972	0.0133151984592
chr1	1000001	1250000	0.0667134614676	-0.0153965230636	-0.00574097879679

PLEASE NOTE, each gap between start and end should be a fixed bin size. ALL BIN SHOULD HAVE AN EIGENVALUE.

Gene Track File Format

We embed the IGV browser into our APP, so all track files are consistent with igv requirements.

[Here is a simple summary.](#)

Track Type	Description	File Formats
annotation	Non-quantitative genome annotations such as genes. T...	bed, gff, gff3, gtf,...
wig	Quantitative genomic data, such as ChIP peaks and al...	wig, bigWig, bedGraph
alignment	Sequencing read alignments.	bam, cram
variant	Genomic variants.	vcf
seg	Segmented copy number data.	seg
mut	Mutation data, primarily from cancer studies.	maf, mut
interact	Arcs representing associations or interactions betwe...	bedpe, interact, big...
gwas	Genome wide association data (manhattan plots)	gwas, bed
arc	RNA secondary structure	bp, bed
junction	RNA splice junctions	bed

Go to [IGV](#) for more details.

3D Structure format

Below is a sample of 3D file ([tab-delimited](#)) or you can [download](#) it.

```
TITLE  'human_coord.3d'      # Tab split, File extension is not required
GENOME hg38      # Tab split
BINSIZE 20000    # Tab split
CHR chr1 # Tab split
0,-2534.13,-654.40,2956.27
1,-2456.07,-620.22,3420.28
2,-2172.37,-688.99,3073.28
3,-1772.57,-889.97,3224.16
4,-1304.49,-924.26,3278.24
5,-1259.02,-825.52,3074.58
6,-1218.38,-1288.18,2971.38
..
CHR chr2
..
```

PLEASE NOTE, ALL BIN SHOULD HAVE A COORDINATES.

This means that the number of the first column is continuous(using nan for those can't calculate coordinates).