Nucleosee is a pattern-search oriented genome browser

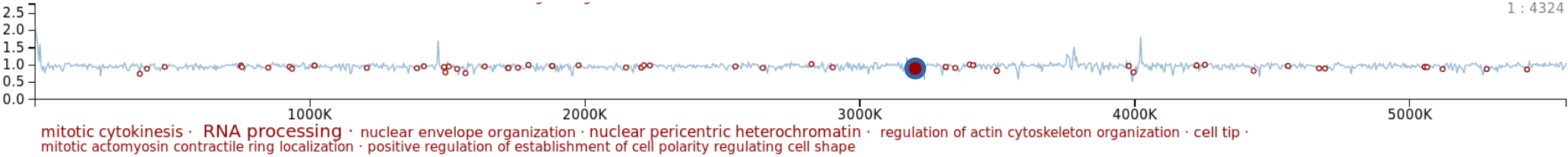
OVERVIEW

Nucleosee has *three levels* which unfold with the pattern search narrative

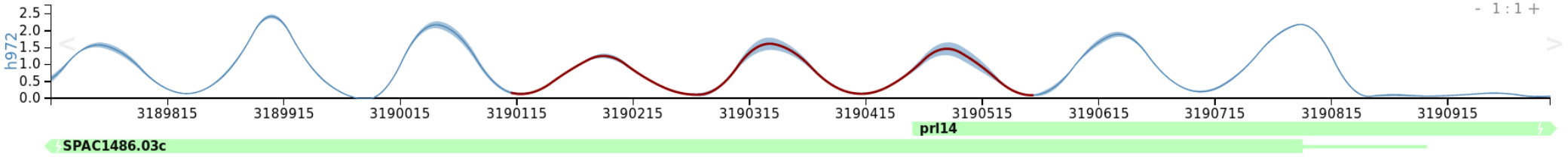
1) Genome level: overall display and pattern matches per chromosome, plus search results download

matches>**58** 62 45 genes>go>fasta>

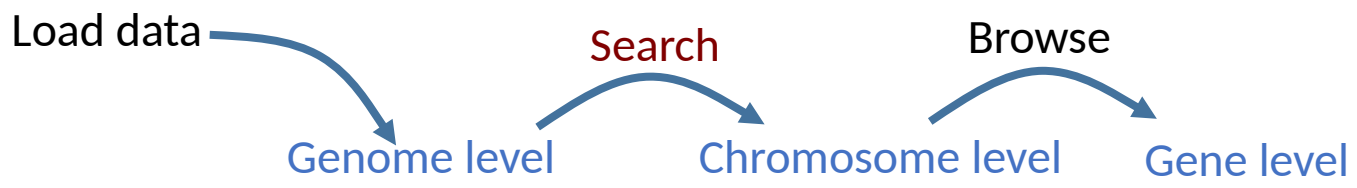
2) Chromosome level: whole single chromosomes for overview and search context



3) Gene level: single search matches are represented on a 1:1 pixel-nucleotide scale base



Typical usage goes like this:



1) Genome level

This level shows the whole dataset as an array of chromosome icons
To load this level, **select data** already preprocessed (see **preprocessing data**) at 

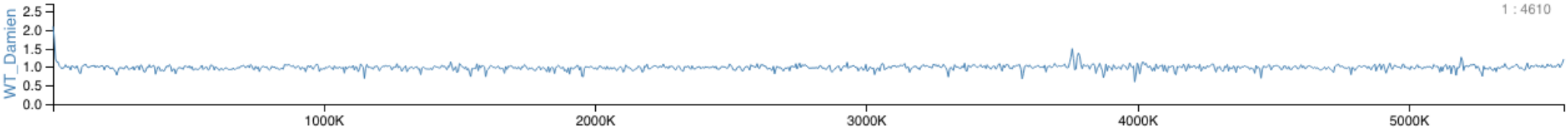

Your chromosomes appear here, the one currently shown at chromosome level is in blue, *click* to change track

Once you perform a **search** (see below), the number of matches on each chromosome, as well as the positions in the current chromosome are highlighted in red.
You can also search by gene name, by GO term (with the prefix `go:`) or by interval (`a-b`)

You can try a working Nucleosee server at http://cpg3.der.usal.es/nucleosee
*Or install your own (see **install your server** below)*

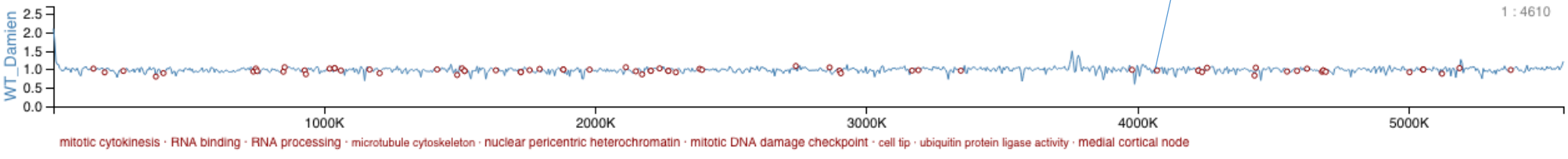
2) Chromosome level

This level shows whole tracks (usually chromosomes) as defined in the coverage files (.wig)
The scale is therefore large, as it only provides the context for searches



Once you perform a **search** (see below), the matching positions in the current chromosome are highlighted in red. You can also search by gene name or GO term (using the `go:` prefix)

Hover over positions to activate the **gene level**



If there are enriched GO terms (FDR<10^{-3}), they are shown here (the larger font the more enriched)
Hover them to see the p-value and the number of annotated genes matching the pattern respect to the total number of annotated genes
Click on them to highlight the annotated genes in the chromosome track.

If you load several datasets, they will appear superimposed in this track, in different colors

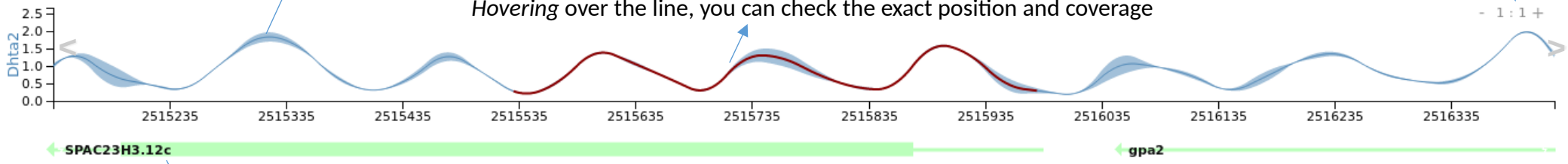
3) Gene level

This level shows a single match on the current search.
It has a 1:1 scale, so each pixel usually represents only one or a few nucleotides:

If you are using data with several replicates (see **preprocessing data**), the variance between replicates will be shown as a shadow below the average line

Click on + - symbols to zoom in or out.
Click on the side arrows to slide through the genome

The section matching your search is higlighted in red
Hovering over the line, you can check the exact position and coverage



Gene annotations are shown here. The wide part corresponds to CDS. The arrow marks the sense.
Hover over the name to see gene details
Click on a gene name to zoom fit to its length.

If you load several datasets, the gene level will show a separate track for each of them

SEARCH

Nucleosee uses BWT to index .wig or .bw data and then perform quick searches.
During preprocessing, numerical levels are split into *windows* and then discretized into *percentile* bins. Each of these bins is represented by a letter (`a`, `b`, `c`, etc.)

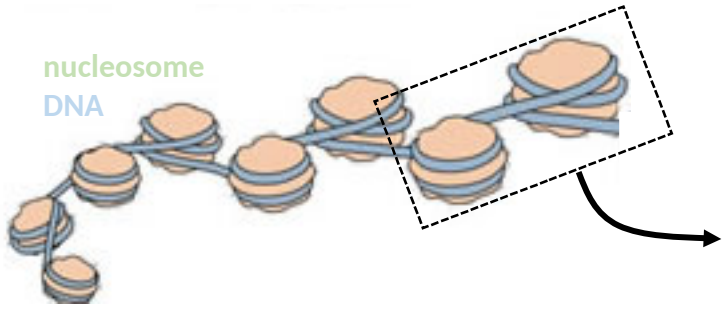
Example 1:

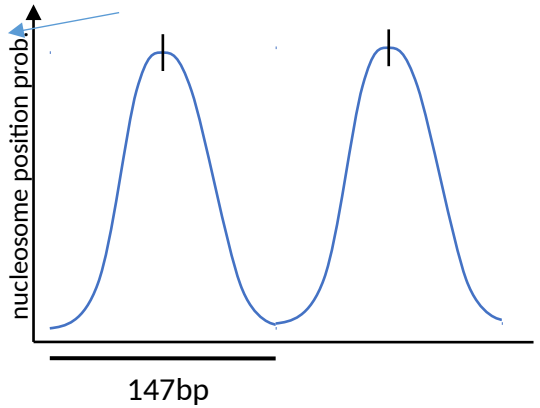
Let be the 10-nucleotide sequence of abundance levels: `1 4 8 9 9 7 6 5 3 0`
A 2-nucleotide window will average it as: `2.5 8.5 8.0 5.5 1.5`
A 3-bin discretization will do: `a c c b a`

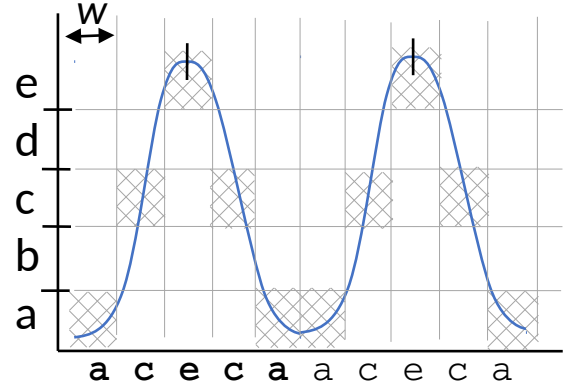
a represents a window value between percentile 0% and 33%, **b** between 33% and 66% and so on.
(with 3 levels, it can be easily memorized as below, around and above average)

Example 2:

For *S pombe* nucleosome maps, a good window choice can be w=`30` bp and d=`5` percentiles
This way, a perfectly positioned nucleosome will be represented as `aceca`, and NDRs as `poly-a`
Or you could simplify the model to w=`50` and `d=3` to characterize nucleosomes as `aca`







SEARCH OPTIONS abcba*2 Search Options

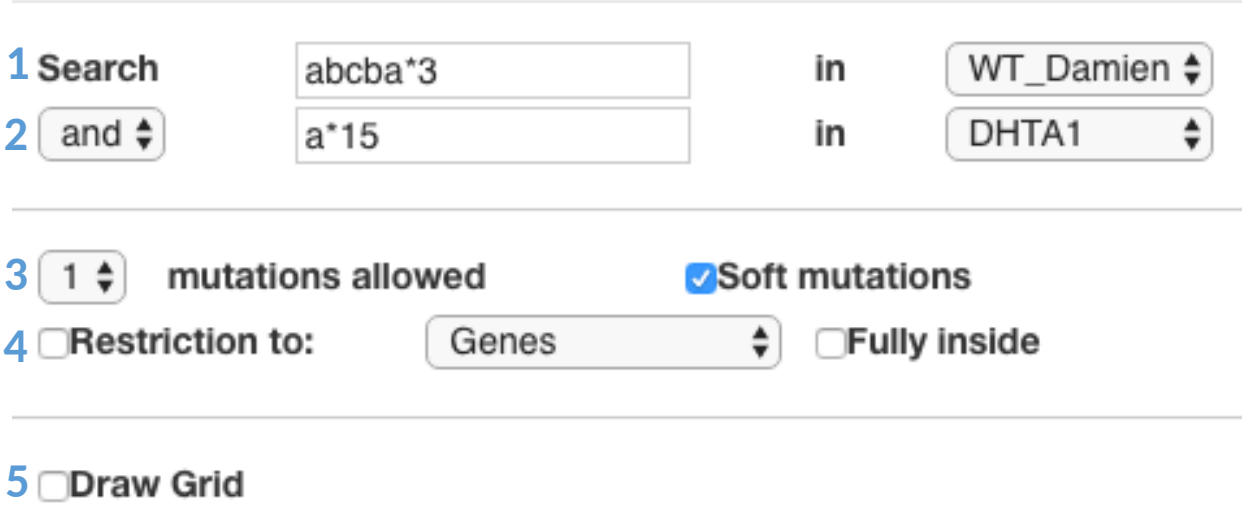
1 **Pattern definition** may include any combination of bin letters and operators `+` and `*`, por example `abcba*3` or `a*5+abcba`. You can also search for gene names or go terms (with the `go:` prefix)

2 **Pattern combination:** in the case of several loaded data sets, we can combine searches of different patterns on them, with different join actions (`and`, `or`, `not`)

3 **Mutations:** number of allowed 1-letter 'variations' from the pattern. As in BWT alignment, a high number of mutations severely affects performance
Soft mutations are changes to a *contiguous* character (`a` to `b` but not `a` to `e`)

4 **Restriction** to especific annotations (genes, UTRs, intergenic regions, etc.) can be applied.
Fully inside restrictions imply that the pattern must fall totally inside the given annotation.

5 **Draw grid** shows the percentile thresholds that separate bins.



Further instructions

Data preprocessing

Setting up a server

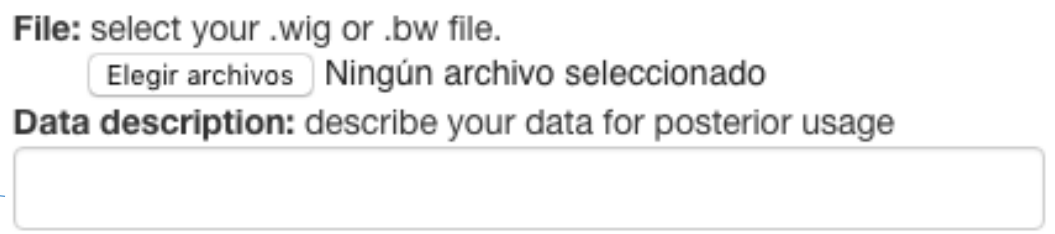
DATA PREPROCESSING

Load file

A link at the top-right of the browser allows the user to load and index .wig or .bw files.
It's recommended to be done by the person that will oversee the server.

You can select one or more files, providing they have the same track names and sizes
They will be batched together and averaged for visualization

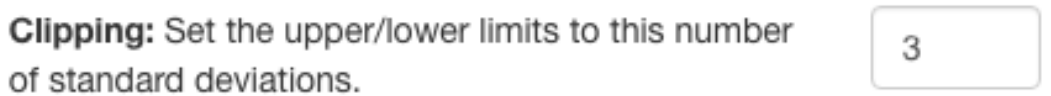
This is the description by which your processed data will be presented to the users when loading data



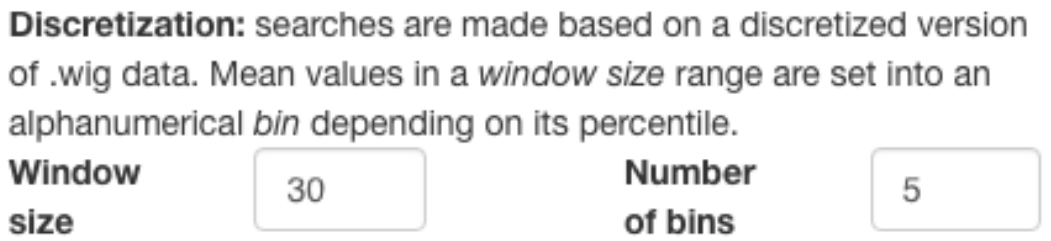
You must select an organism for annotations, enrichment and sequences. You must have previously loaded the organism annotations as explained in **Docker Run Parameters**

.wig files might have variable steps. In such a case, you can choose a way to interpolate missing values

To deal with outliers, you can clip data to remove values above/below a given number of standard deviations



Window size and number of bins refer to the indexing done for searches. See **Search** for more information



SETTING UP NUCLEOSEE

A running Nucleosee server is available for tests at http://cpg3.der.usal.es/nucleosee
Nucleosee is developed as a Docker container for easy server setup at custom locations.

1) Install Docker

Visit https://docs.docker.com/install/ to install Docker on your machine.

2) Setup host folders

Download the annotations folder at http://vis.usal.es/rodrigo/nucleosee/annotations.zip
Unzip it at your preferred location (`ann_path`). You can check its folder structure and add your own organism annotations.

Optionally, you can download some preprocessed examples at
http://vis.usal.es/rodrigo/nucleosee/genomes.zip
Unzip it at your preferred location (`gen_path`)

3) Run Docker container

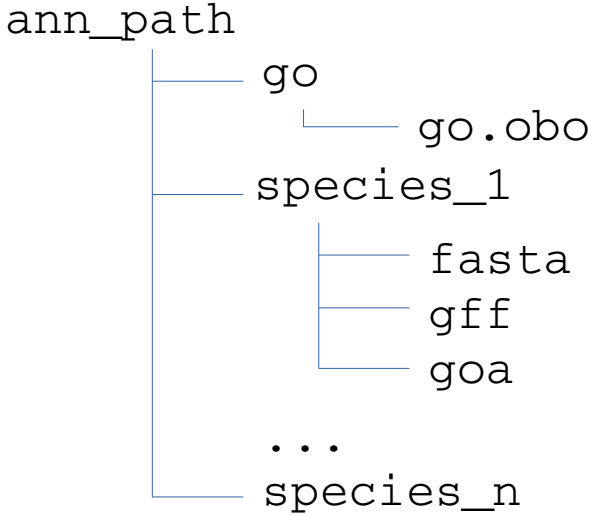
```
docker run -it --rm -p 80:80 -v ann_path:/app/annotations -v
gen_path:/app/genomes -e SERVERNAME=hostname efialto/nucleosee
```

DOCKER RUN PARAMETERS

1) `hostname` is the name of your machine. For example `signus.unas.uk`
2) `ann_path` is the location where you unzipped the example folder in step 2 above, or any other folder you had with the proper structure (see below)
3) `gen_path` is the location where preprocessed data will be stored, along with a file with all your preprocessed data details (`tracks.txt`)

These two last folders (called *volumes* in Docker) will be modified by Nucleosee container itself, and cannot be erased as usual. You should use `docker volume ls` to see which ones have you defined and `docker volume rm volume_name` to delete.

The annotation folder must have the following structure:



This OBO file contains the generic GO term details and can be downloaded from http://geneontology.org

You can name each species as you wish, and populate or not each of the three subfolders with single files for:

- *Genome sequences in fasta format.*
- *Gene annotations in gff format.*
- *GO annotations in gaf format.*

Make sure that gff, fasta and wig files use the same chromosome names. If any file is missing, preprocessing won't use the corresponding information.