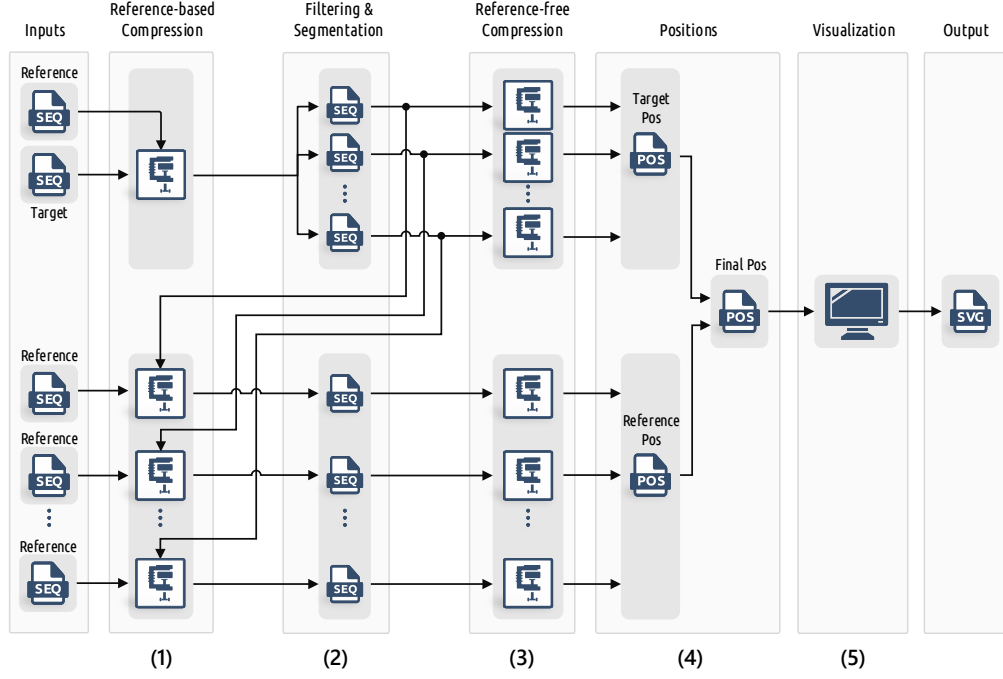


## Note S1 Methods

The schema of the proposed method is illustrated in Fig. S1. There are five major stages in this method, including



**Fig. S1.** The schema of Smash++.

### S1.1 Building models of the data

### S1.2 Finding similar regions

In order to smooth the profile information, we use Hann window [1], which is a discrete window function given by

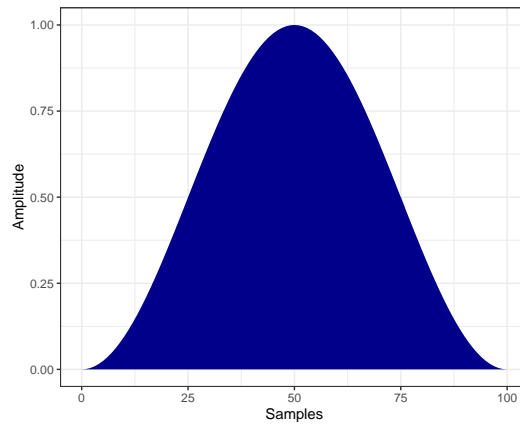
$$w[n] = 0.5 - 0.5 \cos\left(\frac{2\pi n}{N}\right) = \sin^2\left(\frac{\pi n}{N}\right), \quad (\text{Eq. S1})$$

in which,  $0 \leq n \leq N$  and length of the window is  $N + 1$  (Fig. S2).

### S1.3 Computing complexities

### S1.4 The software

Besides Hann window, that is used as default to filter the profile information obtained by the reference-based compression, we have implemented several other window functions (Fig. S3), including Blackman [1], Hamming [2], Nuttall [3], rectangular [4], sine [5], triangular [6] and Welch [7]

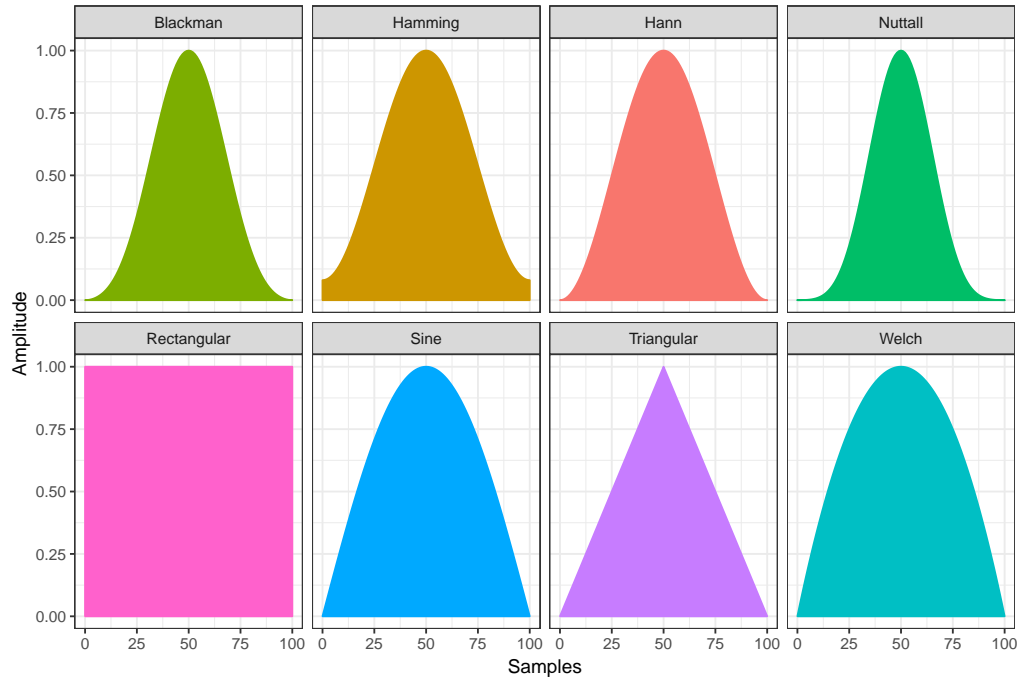


**Fig. S2.** Hann window for 101 samples.

windows. These functions are given by

$$\begin{aligned}
 w[n] &= 1, & (\text{rectangular}) \\
 w[n] &= 1 - \left| \frac{n-N/2}{L/2} \right|, \quad L = N, & (\text{triangular/Bartlett}) \\
 w[n] &= 1 - \left( \frac{n-N/2}{N/2} \right)^2, & (\text{Welch}) \\
 w[n] &= \sin \left( \frac{\pi n}{N} \right), & (\text{sine}) \\
 w[n] &= 0.54348 - 0.45652 \cos \left( \frac{2\pi n}{N} \right), & (\text{Hamming}) \\
 w[n] &= 0.42659 - 0.49656 \cos \left( \frac{2\pi n}{N} \right) + 0.07685 \cos \left( \frac{4\pi n}{N} \right), & (\text{Blackman}) \\
 w[n] &= 0.35577 - 0.48740 \cos \left( \frac{2\pi n}{N} \right) + 0.14423 \cos \left( \frac{4\pi n}{N} \right) - 0.01260 \cos \left( \frac{6\pi n}{N} \right). & (\text{Nuttall})
 \end{aligned}$$

**(Eq. S2)**



**Fig. S3.** Window functions.

## Note S2 Experiment setup

### S2.1 Datasets

**Table S1.** Datasets used in the experiments.

Category	Reference	Length (base)	Target	Length (base)	Description
Synthetic	RefS	1,000	TarS	1,000	
Synthetic	RefM	100,000	TarM	100,000	
Synthetic	RefL	5,000,000	TarL	5,000,000	
Synthetic	RefXL	100,000,000	TarXL	100,000,000	

**Note S3 Results**

Smash++ and several other methods have been carried out on a collection of synthetic and real sequences. The machine used for the tests had an 8-core 3.40 GHz Intel® Core™ i7-6700 CPU with 32 GB RAM.

## Note S4 Tool availability and implementation

Smash++ is implemented in C++ language and is available at [8]. This tool is able to find and visualize rearrangements in sequences, FASTA and FASTQ files; although, it is highly recommended to use sequences as input. In the following sections, we describe installing and running Smash++.

## S4.1 Install

In order to install Smash++ on Linux, run the following commands:

```
1 git clone https://github.com/smortezah/smashpp.git
2 cd smashpp
3 cmake .
4 make
```

## S4.2 Run

A reference file and a target file are clearly mandatory to run Smash++ (without visualization).  
Running

```
1 ./smashpp
```

provides the following guide:

[illegible]

```

42      0: regular (not inverted)
43      1: inverted, solely
44      2: both regular and inverted
45      (FLOAT) a: estimator
46      (FLOAT) g: forgetting factor: [0.0, 1.0)
47      (INT) t: threshold (no. substitutions)

```

The arguments “-r” and “-t” are used to specify the reference and the target, respectively, which are highly recommended to have short names. Level of compression, that is an integer between 0 and 5, can be determined with “-l”. By setting “-m” to an integer value, only those regions in the reference file that are bigger than that value can be considered for compression. Triggering “-nr” makes the tool not to perform the reference-free compression (self-complexity computation) part.

In implementation of the reference-based compression, we have replaced ‘N’ bases in the references and the targets with ‘A’s and ‘T’s, respectively. On reference-free compression, they are replaced with ‘A’s, in both references and targets. If a user tends to replace ‘N’ bases in a sequence with a normal distribution of ‘A’, ‘C’, ‘G’ and ‘T’s, he/she can employ GOOSE toolkit [9]. Note that we have set the entropy of ‘N’s to 2.0, by default, but it is possible for the user to set them to another value of interest, by “-e” option.

Building different finite-context models can be done in the multi-threaded fashion, setting “-n” to an integer. To find similar regions in the reference and the target, information profile (obtained by compression) needs to be filtered, of which the scale can be set as S (small), M (medium) or L (large). Size of the window and type of the windowing function, described in S1.4, can be set by “-w” and “-wt” options, respectively. Instead of considering the complete profile information, the user is able to make samples of it by steps of which size can be determined by “-d”. For the purpose of segmenting the filtered information profile, the average entropy of reference-based compression is used as the threshold, by default. However, this threshold can be altered by “-th” option.

Smash++ accepts FASTA and FASTQ files as input, in addition to sequences. In these cases, the input files are converted to sequences and then processed further. It is possible to save these sequences by “-sb” option.

After obtaining the information profile, Smash++ filters it and then removes it, by default. However, it is possible to save the profile by “-sp” option. The same thing happens to the filtered file, i.e., it is segmented and then is removed. But, the user can use “-sf” to save the filtered file. Also, the segmented files can be saved using “-ss”. The user can save all the information profile, filtered and segmented files, by triggering “-sa” option.

For the purpose of compression, either reference-based or reference-free, it is recommended to use “-l” option, since it configures the models automatically. However, using “-rm” and “-tm”, the user would be able to manually configure the reference model, for reference-based compression, and the target model, for reference-free compression. Parameters of the models are described in detail in section S1.

Running Smash++ (without visualization), positions of the similar regions in the reference and the target, and also complexity of the regions is saved in a “\*.pos” file. To visualize this file, one can type

```

1  ./smashpp -viz

```

which gives

```

1  SYNOPSIS
2  ./smashpp -viz  OPTIONS...  -o SVG-FILE  POS-FILE
3
4  SAMPLE
5
6  DESCRIPTION
7  Mandatory arguments:
8  POS-FILE              positions file, generated by
9                        Smash++ tool (*.pos)
10
11  Options:
12  -v,  --verbose        more information

```

```

13  -o, --out SVG-FILE      output image name (*.svg)
14  -rn, --ref-name STRING  reference name shown on output. If name
15                          has space, use "s, e.g. "Seq label".
16                          Default: name in header of position file.
17  -tn, --tar-name STRING  target name shown on output
18  -vv, --vertical         vertical view
19  -nn, --no-nrc           do NOT show normalized
20                          relative compression (NRC)
21  -nr, --no-redun         do NOT show self complexity
22  -ni, --no-inv           do NOT show inverse maps
23  -ng, --no-reg           do NOT show regular maps
24  -l, --link INT          type of the link between maps: [1, 6]
25  -c, --color INT         color mode: [0, 2]
26  -p, --opacity FLOAT     opacity: [0.0, 1.0]
27  -w, --width INT         width of the sequence: [15, 100]
28  -s, --space INT         space between sequences: [15, 200]
29  -f, --mult INT          multiplication factor for
30                          color ID: [1, 255]
31  -b, --begin INT         beginning of color ID: [0, 255]
32  -rt, --ref-tick INT     reference tick: [1, 4294967295]
33  -tt, --tar-tick INT     target tick: [1, 4294967295]
34  -th, --tick-human 0|1   tick human readable: 0=false, 1=true
35  -m, --min INT          minimum block size: [1, 4294967295]
36  -h, --help             usage guide

```

The output of Smash++ visualizer is an “SVG” file, which its name is determined by “-o” option. By default, it is named “map.svg”. Names of the reference and the target, which are going to be printed on the output image, can be altered by “-rn” and “-tn”, respectively. They are by default the names written in the positions file. To have a vertical view of the image, instead of the default horizontal view, one can use “-vv” trigger.

Smash++ performs reference-based and reference-free compressions to calculate the normalized relative compression (NRC) and redundancy (self complexity), respectively. If the user is not interested in showing them, he/she can turn them off by “-nn” and “-nr” triggers. In addition, Smash++ considers both regular and reverse complement maps by default in its calculations. Triggering “-ni” and “-ng” will stop showing inverted and regular maps, respectively.

Options “-l”, “-c”, “-p”, “-w”, “-s”, “-f” and “-b” can be used to change the appearance of the image. Assigning integers to “-rt” and “-tt” options will change the tick sizes of the reference and the target, respectively. Smash++ prints the sizes on axes in human readable format, e.g., 1K, 2M, etc. However, it can be triggered by “-th” option. Note that, here, 1K is equivalent to 1000 and not 1024. Finally, by setting “-m” to an integer value, only the regions that are bigger than that value will be illustrated.

### S4.3 Example

This section guides, step-by-step, employing Smash++ to find and visualize rearrangements in a sample genomic data.

#### Install Smash++ and provide the required files

First, we install Smash++:

```

1  git clone https://github.com/smortezah/smashpp.git
2  cd smashpp
3  ./compile.sh

```

Then, we copy `smashpp` binary file into `example/` directory and go to that directory:

```

1  cp smashpp example/
2  cd example/

```

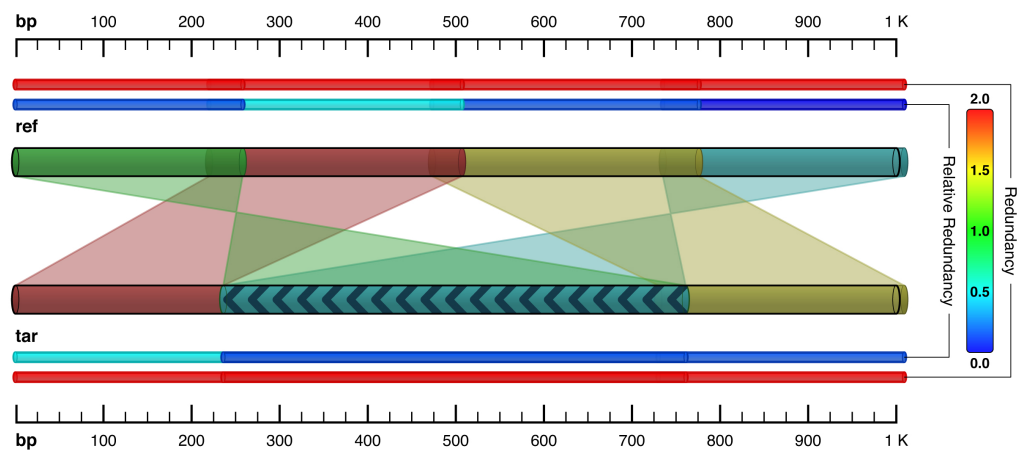
In this directory, a 1000 byte reference sequence, `ref`, and a 1000 byte target sequence, `tar`, are provided. Running

```

1 ./smashpp -r refs -t tars -w 45 -l 3
2 ./smashpp -viz refs.tars.pos

```

results in Fig. S4, which is saved in “map.svg”.



**Fig. S4.** The result of running Smash++ on ...



## References

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- [8] M. Hosseini, D. Pratas, and A. J. Pinho. Smash++. [Online]. Available: <https://github.com/smortezah/smashpp>
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