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Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see <u>Authors & Referees</u> and the <u>Editorial Policy Checklist</u>.

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For	all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.
n/a	Confirmed
x	The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
x	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
x	The statistical test(s) used AND whether they are one- or two-sided Only common tests should be described solely by name; describe more complex techniques in the Methods section.
x	A description of all covariates tested
x	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
x	For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
x	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
x	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
x	Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i>), indicating how they were calculated
	Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection

For downloading and preprocessing of the public datasets:

GitHub: https://github.com/wkopp/janggu_usecases/tree/master/00_preparation

Data analysis

Janggu package source code:

GitHub: https://github.com/BIMSBbioinfo/janggu
Pypi.org: https://pypi.org/project/janggu/0.9.3/
Archived version: https://github.com/BIMSBbioinfo/janggu/archive/v0.9.3.tar.gz

Supplementary code to run the use cases:

GitHub: https://github.com/wkopp/janggu_usecases
Archived version: https://github.com/wkopp/janggu_usecases/archive/v1.0.0.tar.gz

Additional:
samtools (1.9), bedtools (2.29)

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about <u>availability of</u> data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

For use case 1 we used:

https://www.encodeproject.org/files/ENCFF446WOD/@@download/ENCFF446WOD.bed.gz

https://www.encodeproject.org/files/ENCFF546PJU/@@download/ENCFF546PJU.bam

https://www.encodeproject.org/files/ENCFF059BEU/@@download/ENCFF059BEU.bam

http://mitra.stanford.edu/kundaje/akundaje/release/blacklists/hg38-human/hg38.blacklist.bed.gz

http://hgdownload.cse.ucsc.edu/goldenPath/hg38/bigZips/hg38.fa.gz

For use case 2 we used:

 $narrow Peak files in \ https://github.com/wkopp/janggu_usecases/tree/master/extra/urls.txt (archived \ version \ v1.0.0)$

http://hgdownload.cse.ucsc.edu/goldenPath/hg19/bigZips/hg19.fa.gz

For use case 3 use obtained:

https://www.encodeproject.org/files/ENCFF591XCX/@@download/ENCFF591XCX.bam

https://www.encodeproject.org/files/ENCFF736LHE/@@download/ENCFF736LHE.bigWig

ftp://ftp.ebi.ac.uk/pub/databases/gencode/Gencode human/release 29/gencode.v29.annotation.gtf.gz

https://www.encodeproject.org/files/ENCFF177HHM/@@download/ENCFF177HHM.bam

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Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.						
x Life sciences	Behavioural & social sciences Ecological, evolutionary & environmental sciences					
For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf						
Life sciences study design						
All studies must dis	close on these points even when the disclosure is negative.					
Sample size	Only previously published data were used. Sample size as in classical statistical testing is not relevant for this study.					
Data exclusions	Only previously published data were used. No data was excluded.					
Replication	The study does not present experimental findings.					
Randomization	This study does not present experimental findings.					
Blinding	We did not need blinding since we had no randomized control trials. The concept is irrelevant for our study as we did not perform					

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

experiments and the experiments we used for the use cases did not include treatment, they were observational.

Materials & experimental systems		Methods		
n/a	Involved in the study	n/a Involved in the s	tudy	
X	Antibodies	ChIP-seq		
×	☐ Eukaryotic cell lines	Flow cytometr	ry	
×	Palaeontology	MRI-based ne	uroimaging	
x	Animals and other organisms	·		
x	Human research participants			
×	Clinical data			