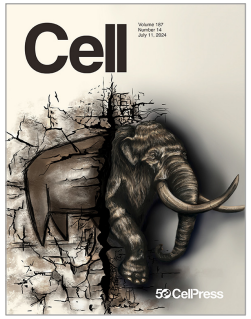
Picture from the book: Castells i Castellers. Una voluntat col·lectiva.

Fossilized chromosomes from woolly mammoth

Marc A. Marti-Renom

CNAG-CRG · ICREA

Cell. Volume 187 (14) July 11, 2024.



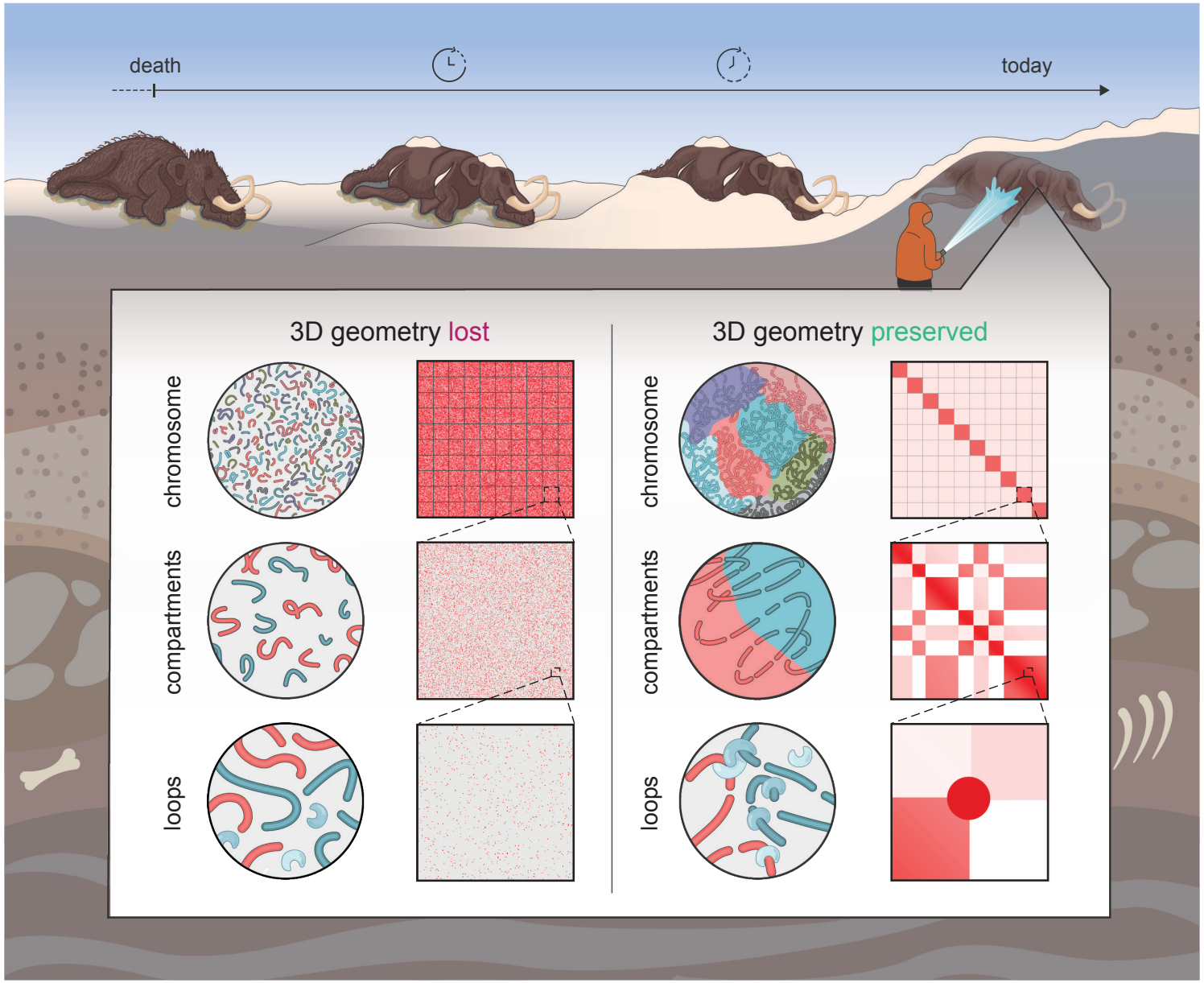
Marcela Sandoval Velasco
(ex) Gilbert Lab

Olga Dudchenko
Aiden Lab

Juan Antonio Rodríguez
(ex) Marti-Renom Lab

Cynthia Perez Estrada
(ex) Aiden Lab

What happens to the nucleus in 10s of thousands of years?



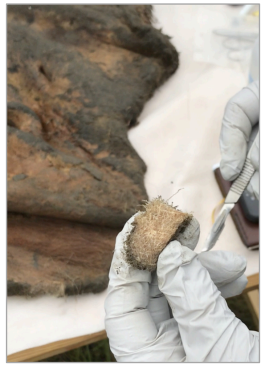
A “whoolly” phenomenal sample

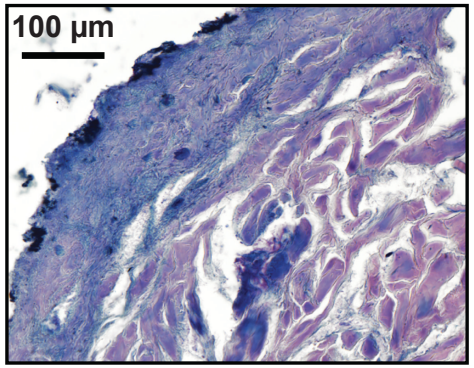
Photo credit: Chris Waddle

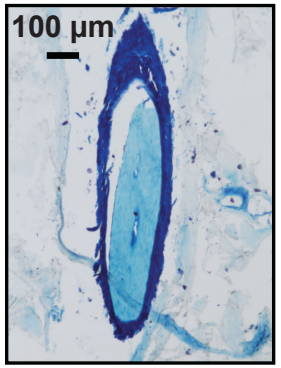
Dan Fisher
UMich, Museum of Paleontology

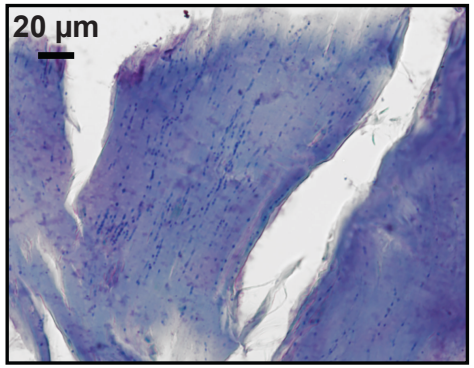
Valeri Plotnikov
Sakha Academy of Sciences

- Found in permafrost in the summer of 2018
- Belaya Gora in Yakutia, Russia
- Date >45,000 years









Paleo-HiC complements ancient DNA-seq

Limitations of (a)DNA-Seq

What is in the genome?

Need chrom-length de novo assemblies!
aDNA-Seq relies on modern references

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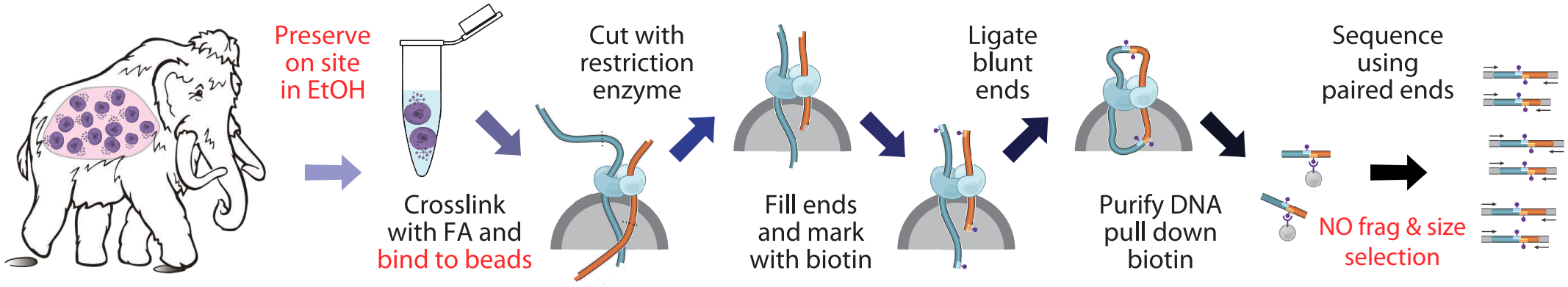
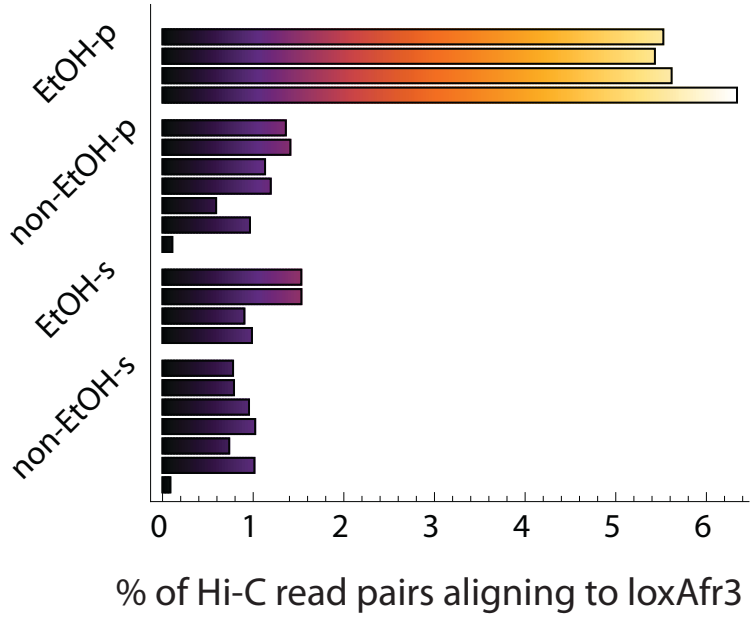
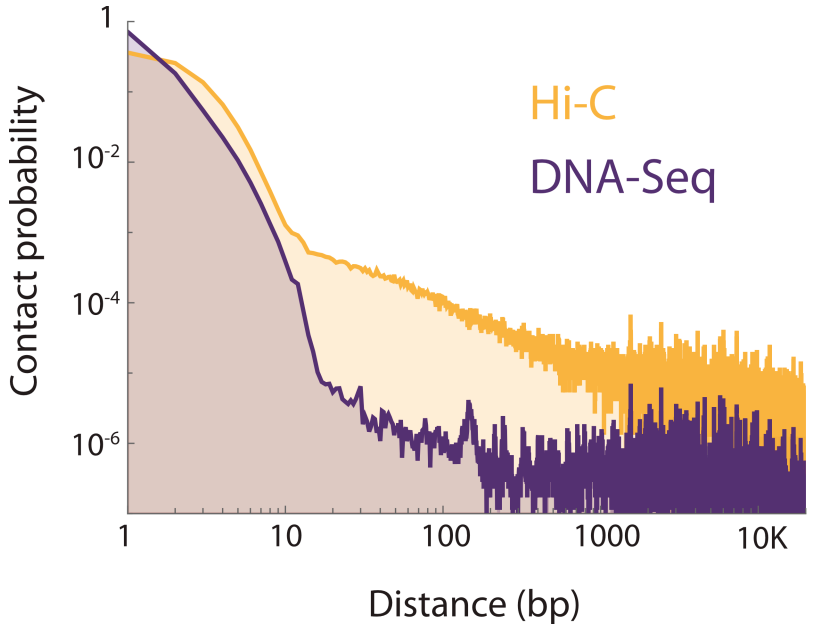
Paleo-HiC improves endogenous long-range contact recovery



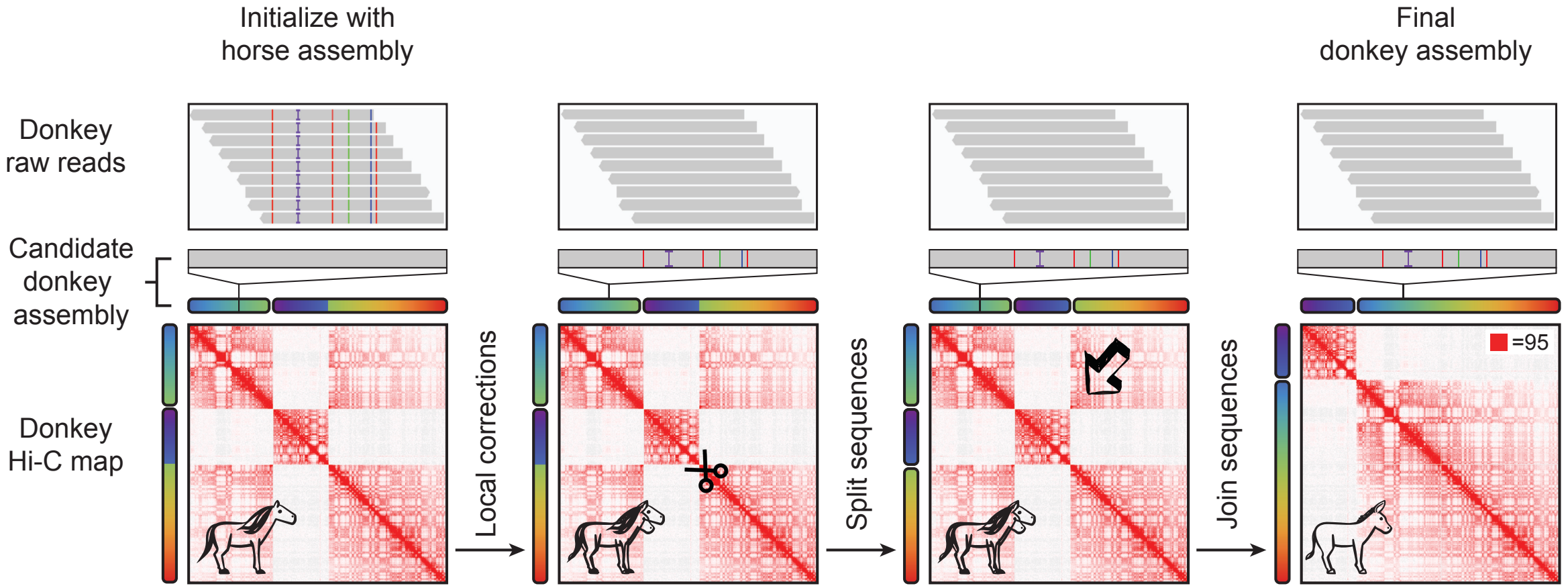


Total read count	4,444,894,354
Unique paired alignments (loxAfr3)	24,415,411
Unique paired (%)	0.55%
Long-range (20kb)	1,763,225
Long-range (%)	0.04%



Hi-C assisted assembly

Dubchenko et al. Science. 2017 Apr 7;356(6333):92-95

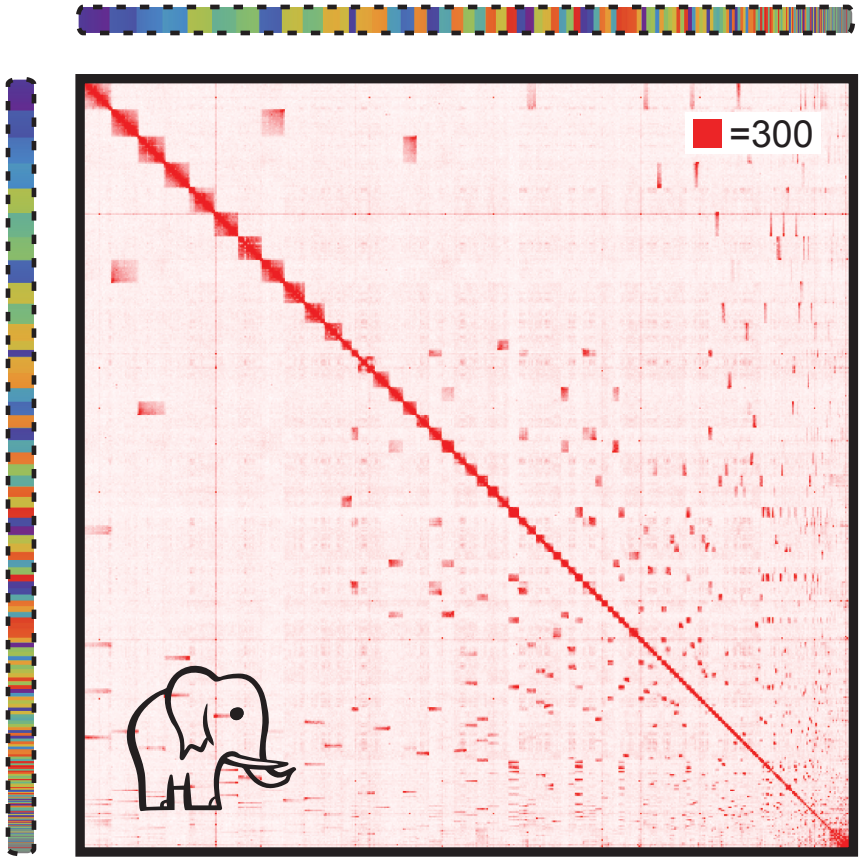


correct · split · orient · order

This is a Hi-C from mammoth

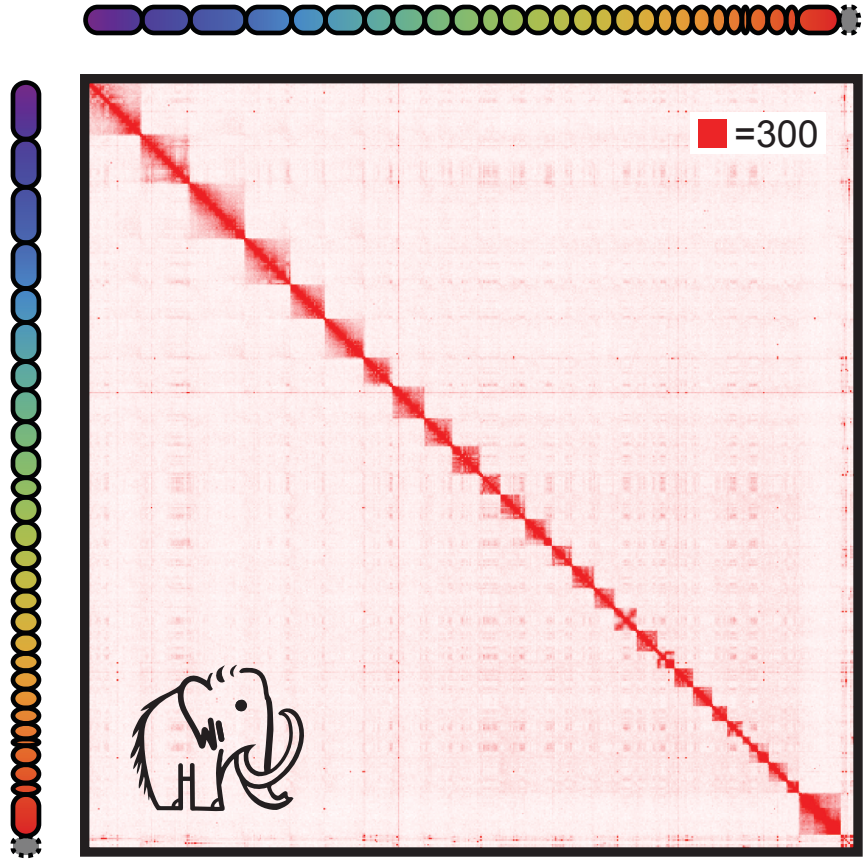
based on Loxafr3.0

PaleoHi-C vs Loxafr3.0,
fragmentary African elephant assembly



3D assisted
assembly

PaleoHi-C vs MamPri_Loxafr3.0_assisted_HiC,
chromosome-length mammoth assembly



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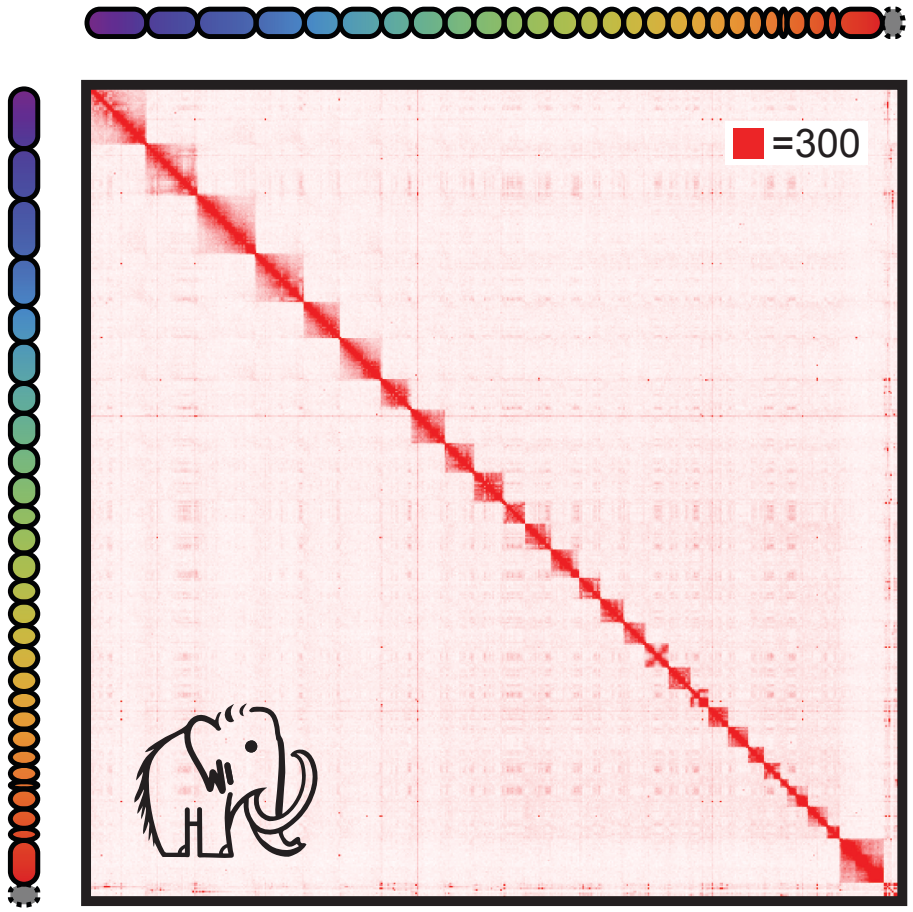
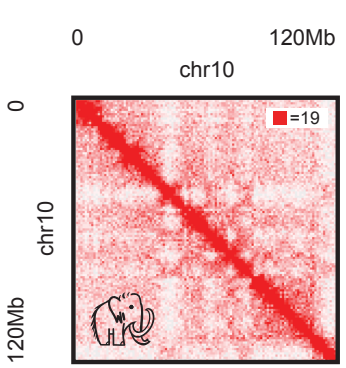
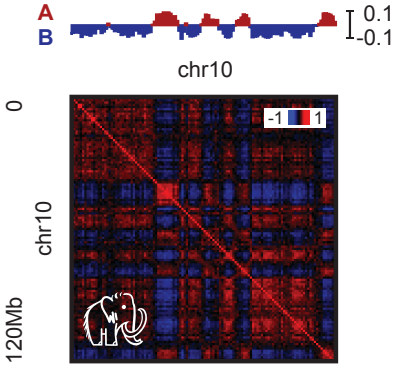
- Chromosome territories

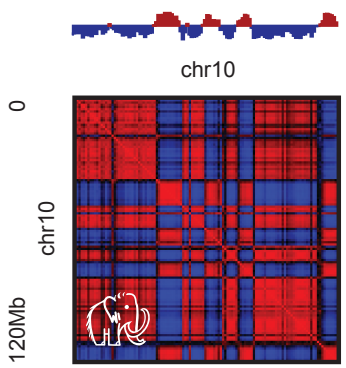
Facilitates **de novo assembly of whole chromosomes**

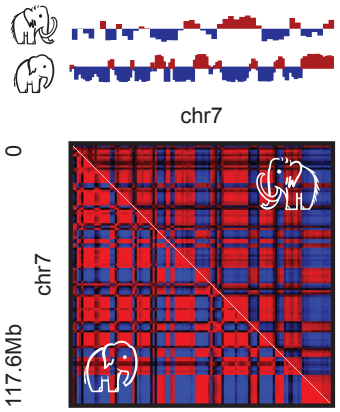
Compartments preserved in a 52K years old sample

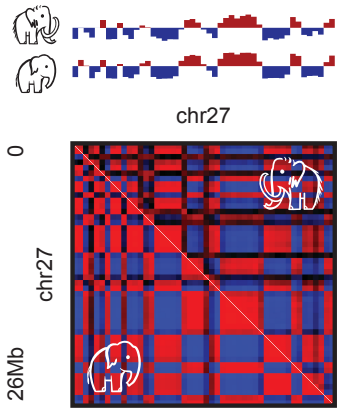


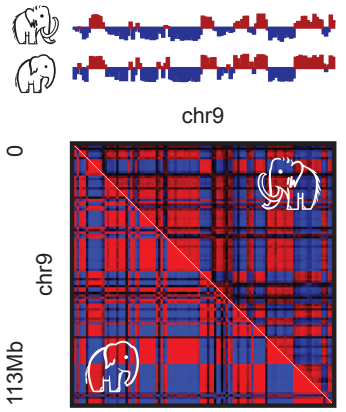




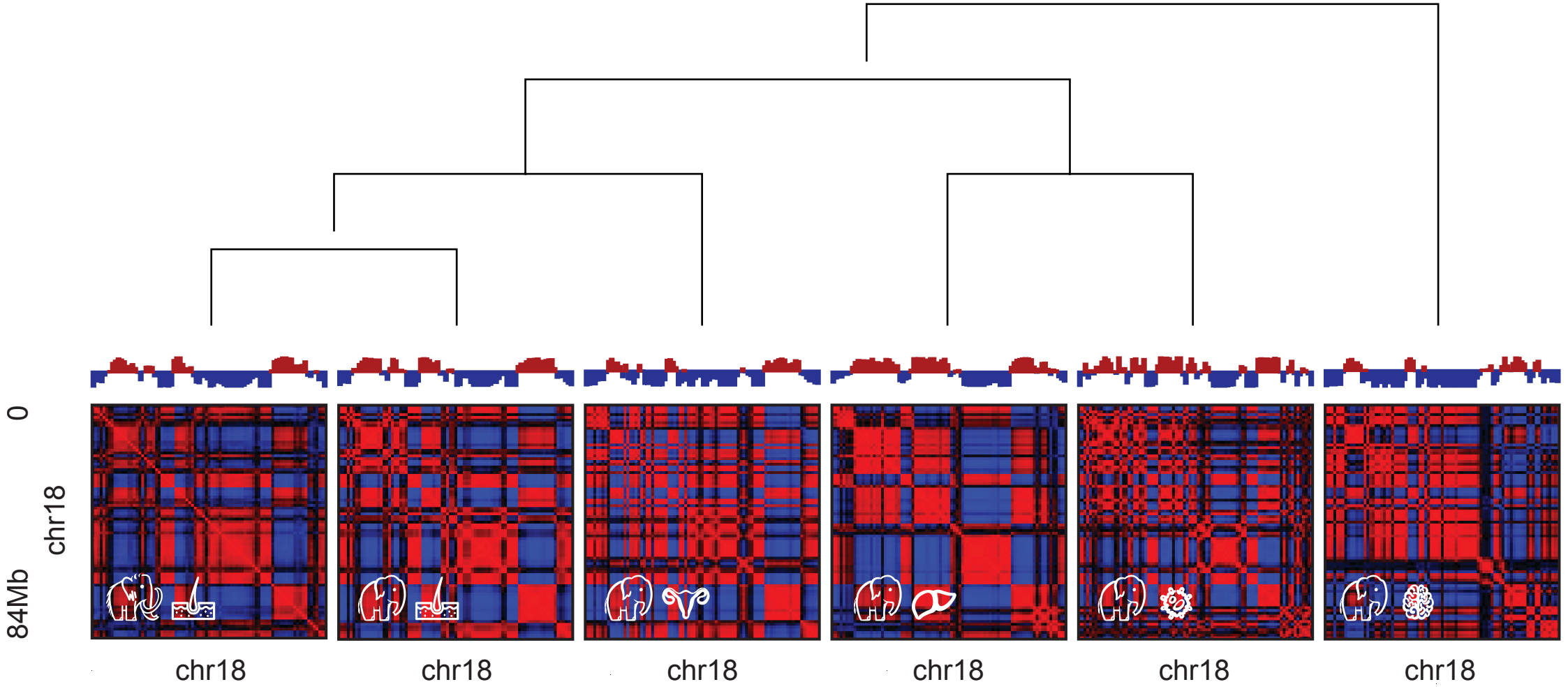




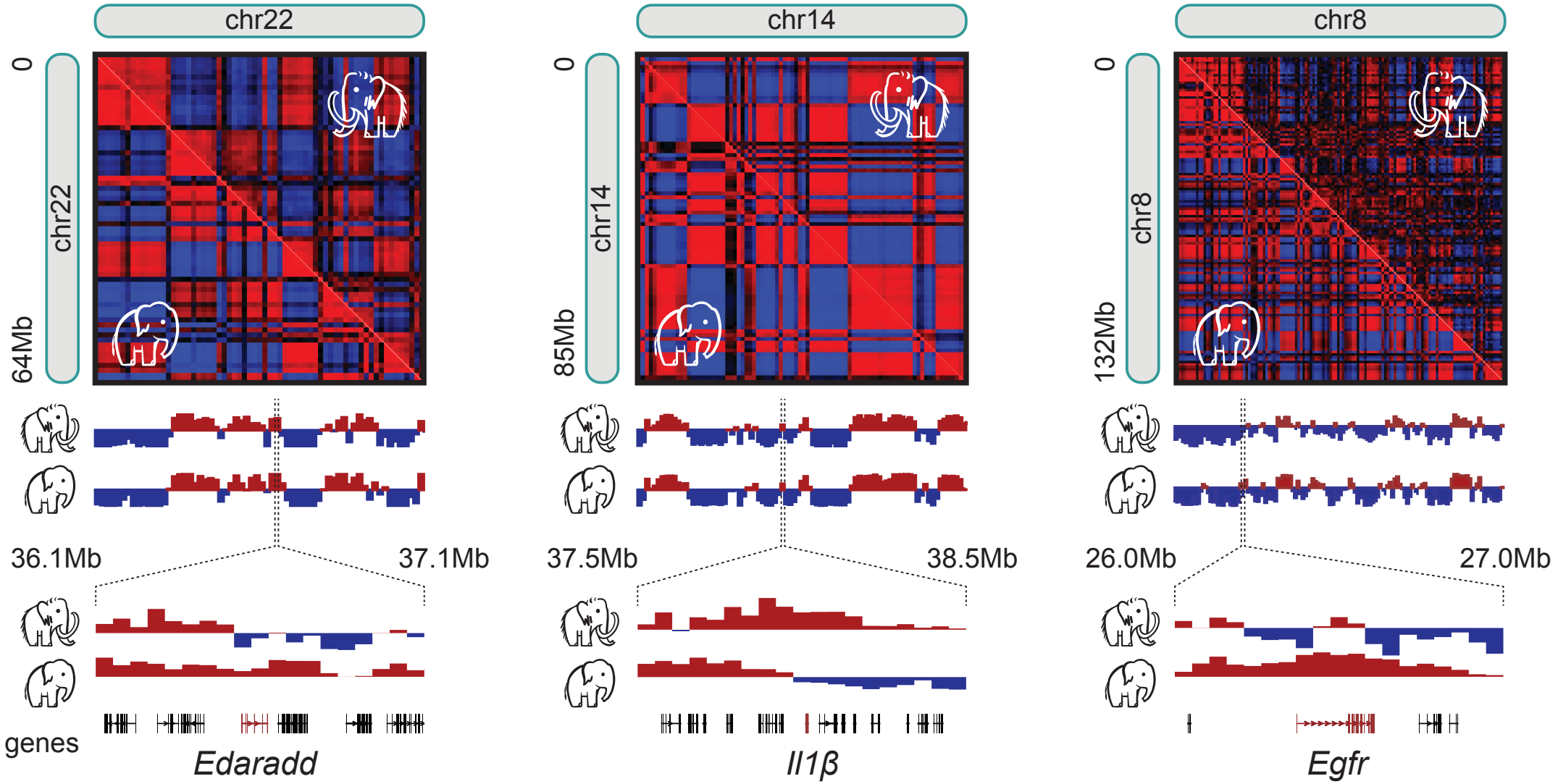




Tissue specific compartmentalization



Mammoth Altered Regulation Sequences (MARS)



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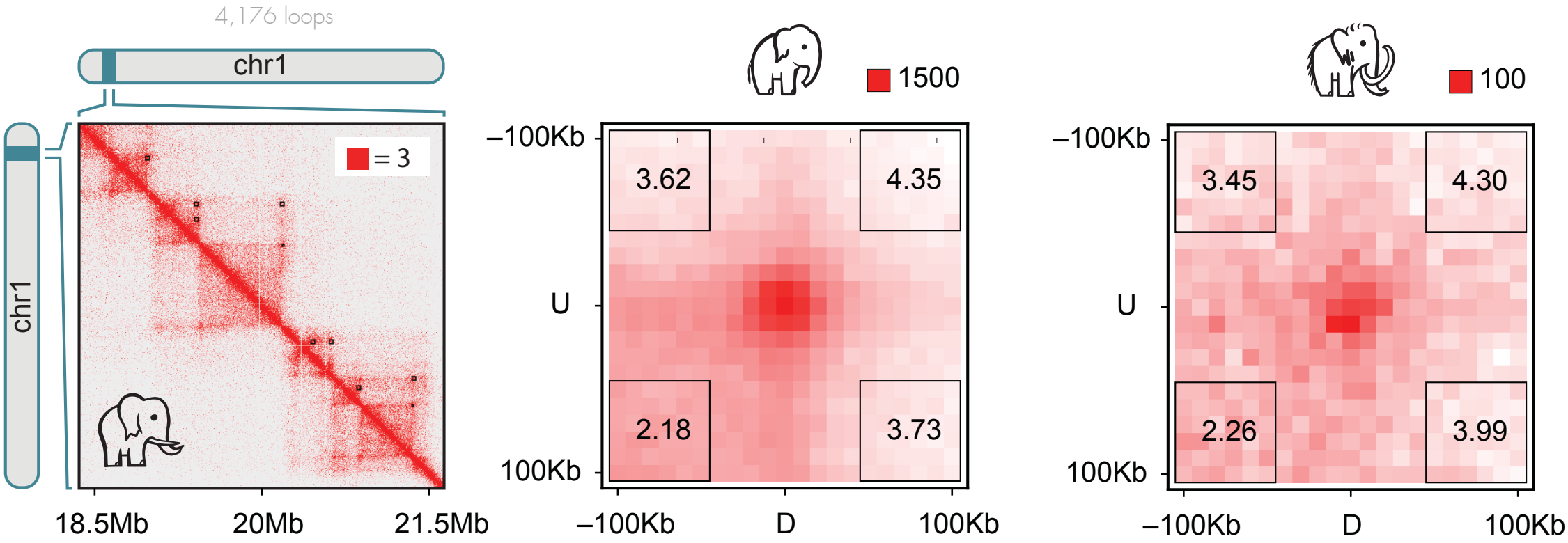
- Active and inactive chromatin compartments
  Probes **Transcriptional activity**

Paleo-hic recovers loop signatures!

Rao, Huntley et al., Cell 2014



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- Active and inactive chromatin compartments
  Probes **Transcriptional activity**

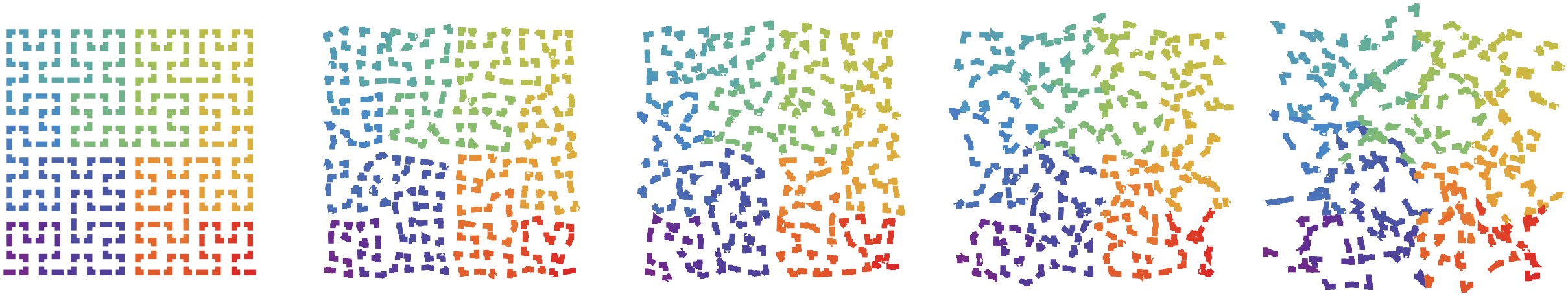
- Chromatin Loops
  Reveals **regulation of individual genes**

How is this possible? (q.k.a. reviewer #3)

The "chromoglass" hypothesis

Initial structure

Diffusion



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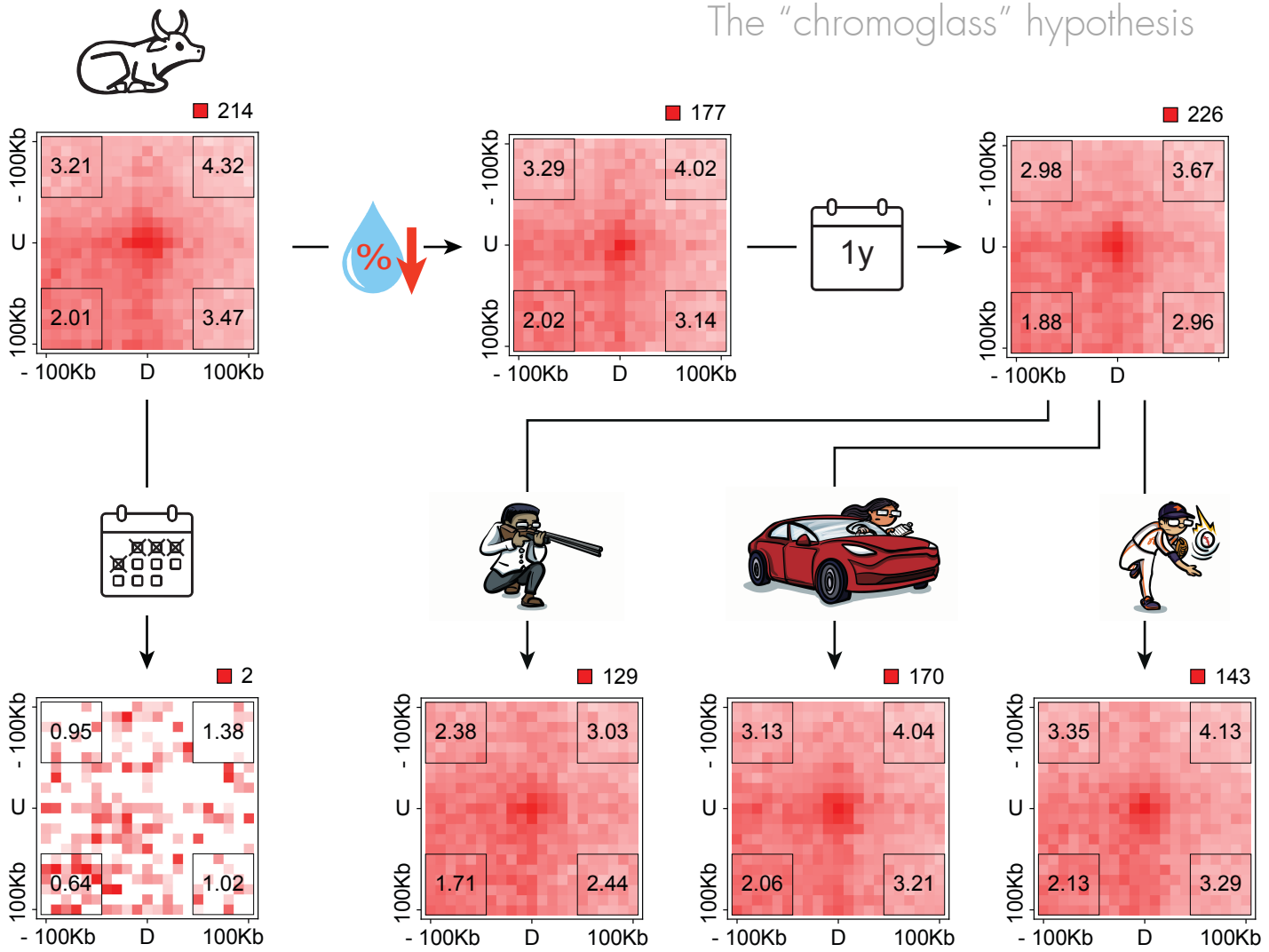

THREE-DIMENSIONAL GENOME ARCHITECTURE PERSISTS IN A 52,000-YEAR-OLD WOOLLY MAMMOTH SKIN SAMPLE

Marcela Sandoval-Velasco[#], Olga Dudchenko[#,†], Juan Antonio Rodríguez[#], Cynthia Pérez Estrada[#], Marianne Dehasque, Claudia Fontsere, Sarah S.T. Mak, Ruqayya Khan, Vinícius G. Contessoto, Antonio B. Oliveira Junior, Achyuth Kalluchi, Bernardo J. Zubillaga Herrera, Jiyun Jeong, Renata P. Roy, Ishawnia Christopher, David Weisz, Arina D. Omer, Sanjit S. Batra, Muhammad S. Shamim, Neva C. Durand, Brendan O'Connell, Alfred L. Roca, Maksim V. Plikus, Mariya A. Kusliy, Svetlana A. Romanenko, Natalya A. Lemskaya, Natalya A. Serdyukova, Svetlana A. Modina, Polina L. Perelman, Elena A. Kizilova, Sergei I. Baiborodin, Nikolai B. Rubtsov, Gur Machol, Krisha Rath, Ragini Mahajan, Parwinder Kaur, Andreas Gnirke, Isabel Garcia-Treviño, Rob Coke, Joseph P. Flanagan, Kelcie Pletch, Aurora Ruiz-Herrera, Valerii Plotnikov, Innokentiy S. Pavlov, Naryya I. Pavlova, Albert V. Protopopov, Michele Di Pierro, Alexander S. Graphodatsky, Eric S. Lander, M. Jordan Rowley, Peter G. Wolynes, José N. Onuchic, Love Dalén, Marc A. Marti-Renom[†], M. Thomas P. Gilbert[†], Erez Lieberman Aiden[†]

Cell 2024

Take home messages:

Mammoth foot
Photo credit: Love Dalén

- Hi-C was done in a 52,000-year-old well conserved sample.
- Chromosome fossils also enable to assemble the entire genome of extinct species.
- Chromosome fossils help to interpret how the genomes of those species were organized in space as well as its functional activity.
- Key mammoth genes associated with hair follicle development were active in mammoth compared to modern elephants.
- Specific loop interactions in the genome regulating gene expression were also visible and conserved in the mammoth sample.
- Chromoglass (a glass-like-state of the chromosomes) allowed the genome structure to be physically conserved over such long period of time.

https://tinyurl.com/MammothPaper

http://marciuslab.org
http://3DGenomes.org

@mamartirenom

Juan Antonio Rodríguez

Marcela Sandoval Velasco

Tom Gilbert

Olga Dudchenko

Cynthia Perez Estrada

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Love Dalén

Jordan Rowley

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Kerstin Lidblad-Toh,
Federica Di Palma et al.

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