

Bilkent University Spring 2025
CS481 Homework Assignment #5

A high-coverage Neandertal genome from Vindija Cave in Croatia*

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*Prüfer, Kay, et al. "A high-coverage Neandertal genome from Vindija Cave in Croatia." *Science*, vol. 358, no. 6363, 3 Nov. 2017, pp. 655–658, <https://doi.org/10.1126/science.aao1887>.

What the paper does – in one sentence

Sequenced a ~50 kyr-old Neandertal femur (Vindija 33.19) to 30× depth, providing the first high-quality European Neandertal genome and refining detection of Neandertal ancestry in modern humans [1].

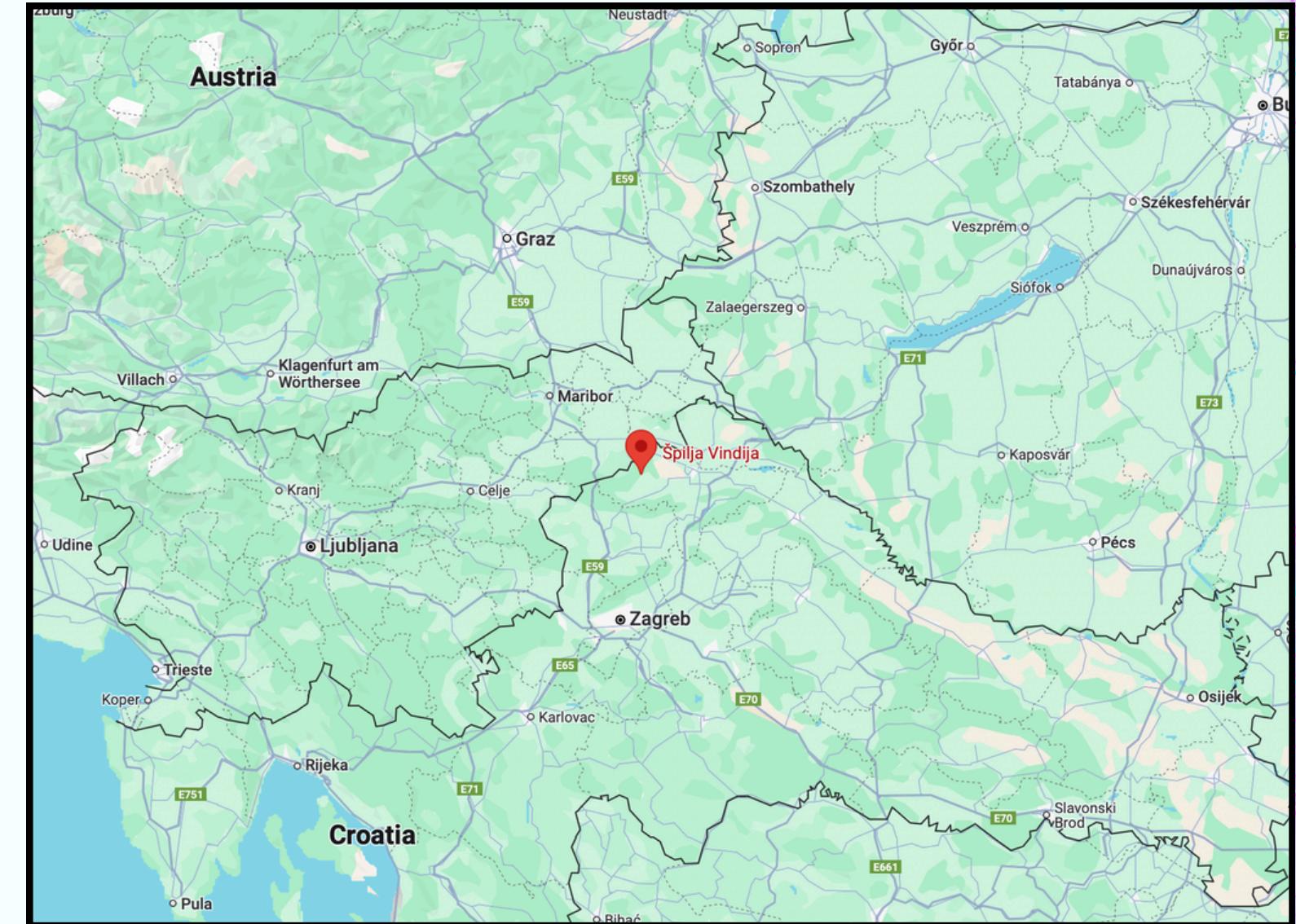


Figure 1: Map of Vindija Cave, Croatia. Google Maps, 2025, maps.google.com.

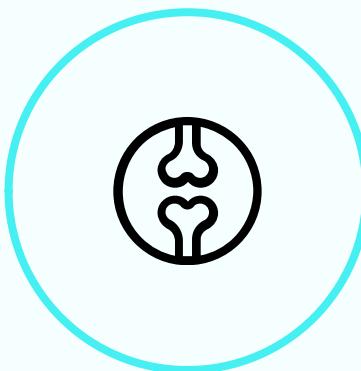
Background – why this matters

- Ancient DNA is scarce, damaged (<60 bp) and prone to contamination [1].
- Before 2017 only one high-coverage Neandertal genome (Altai, Siberia) existed [1].
- Low-resolution European data limited population-genetic and bioinformatics analyses [1][2].

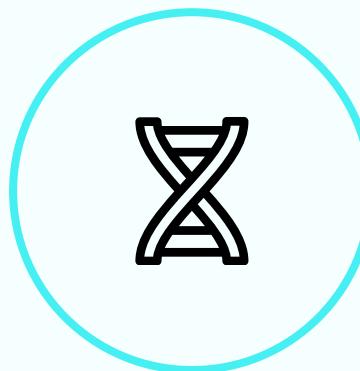


Figure 2: Neanderthal woman reconstruction (Saint-Césaire, France).
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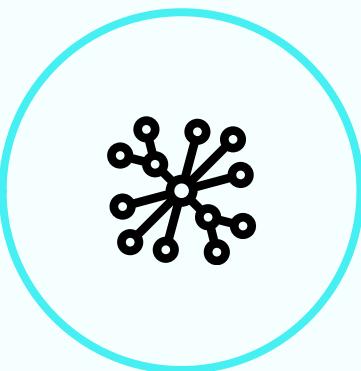
Sample & Chronology



Specimen: cortical
bone fragment
Vindija 33.19,
Vindija Cave,
Croatia [1].



Radiocarbon:
>45.5 ka BP [1].



Excellent DNA
preservation
relative to other
European
Neandertals [1].

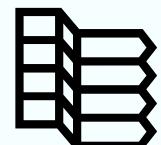
Wet-lab Methods



Powder drilling; EDTA/Proteinase K extraction at low temperature to minimise depurination [1].



Constructed 12 double-stranded Illumina libraries (mostly non-UDG) to retain short, damaged molecules [1].



Generated 24 bn reads; 2.4 bn mapped to hg19 (~10 % endogenous) [1].

Bioinformatics Pipeline

- Adapter-trim & merge, map with BWA-aln (seed disabled) [1].
- Damage-aware genotyping with.snpAD [1].
- Contamination estimates (mtDNA, X-chromosome, ancestry-SNPs) < 1 % [1].
- High depth enabled indel and duplication discovery [1].

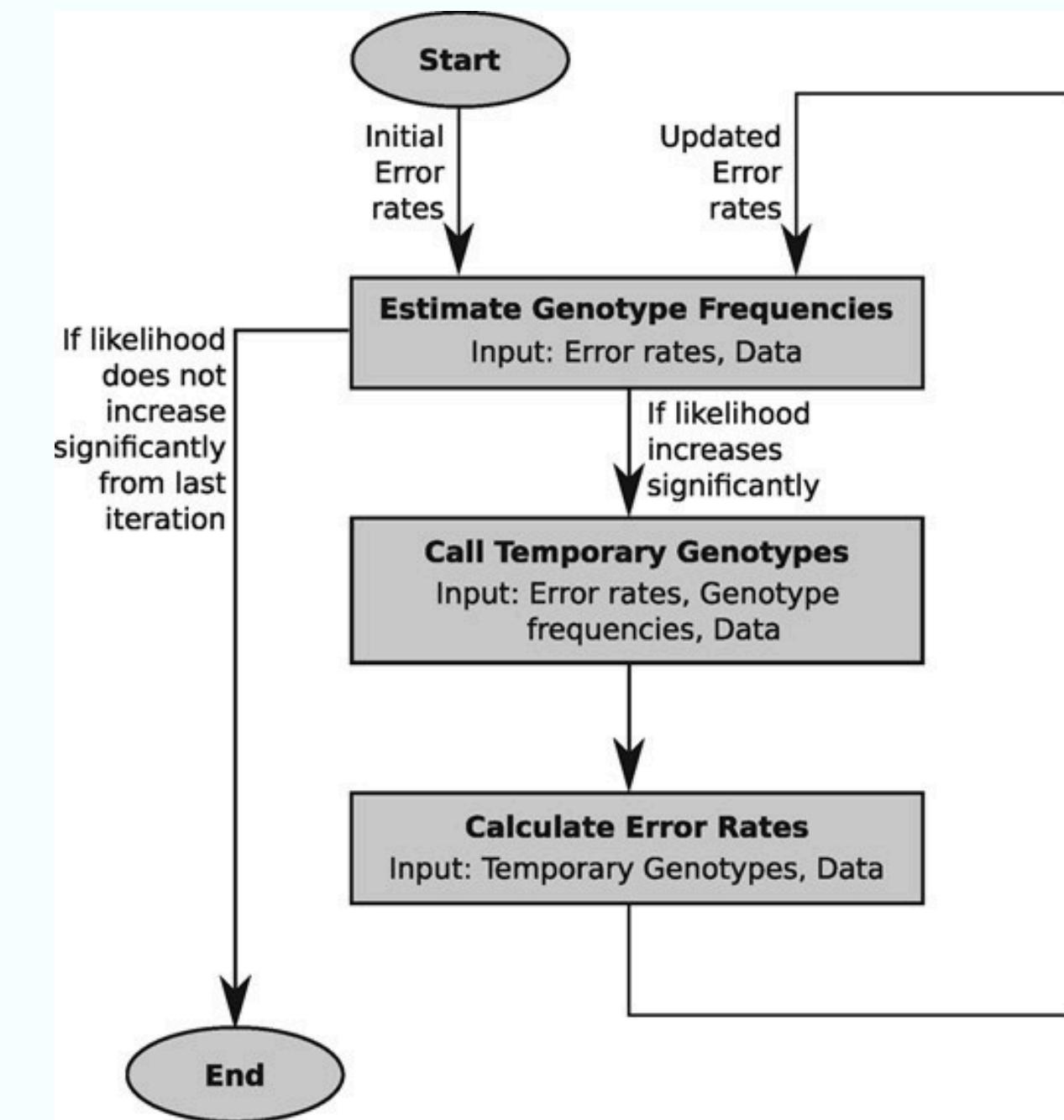
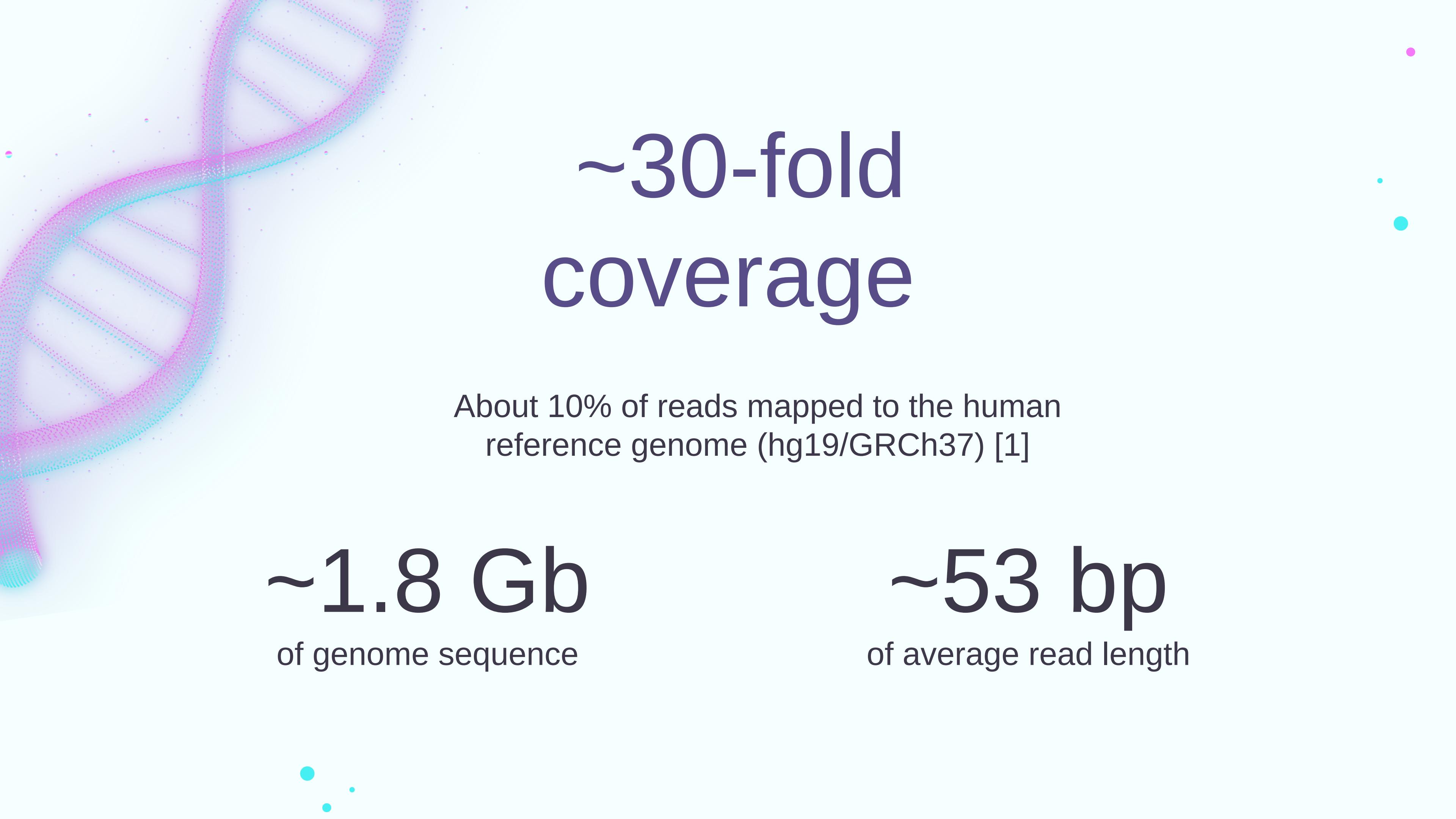


Figure 3: Schematic overview of the method implemented in snpAD [3]



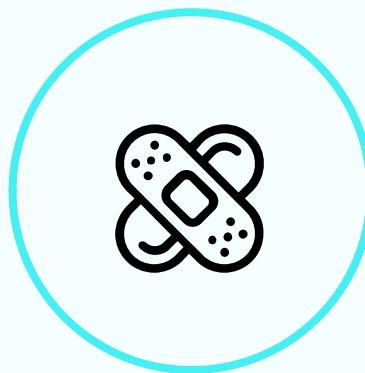
~30-fold coverage

About 10% of reads mapped to the human
reference genome (hg19/GRCh37) [1]

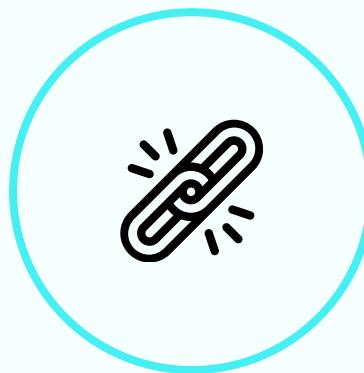
~1.8 Gb
of genome sequence

~53 bp
of average read length

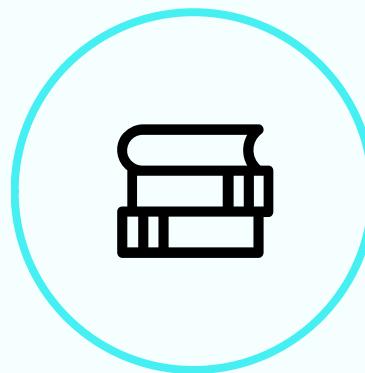
Results



Newly tagged alleles influence LDL cholesterol, immune traits, nicotine addiction, schizophrenia risk [1].



Neandertal-specific duplications found in olfactory-receptor clusters [1].

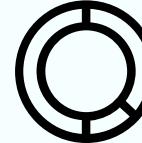


Created a public catalogue of ~4 million Neandertal SNPs [1].

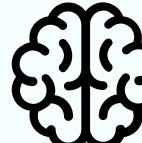
Applications in Bioinformatics



Benchmarking damage-aware aligners
(nf-core/eager, PALEOMIX) [1].



Functional annotation in Ensembl VEP
and PharmGKB [1].



Training data for ML base-calling of ancient
DNA [1].

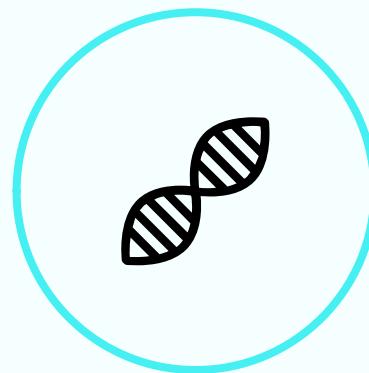


Improved introgression detection (IBDmix,
Sprime, IBIS) [1].

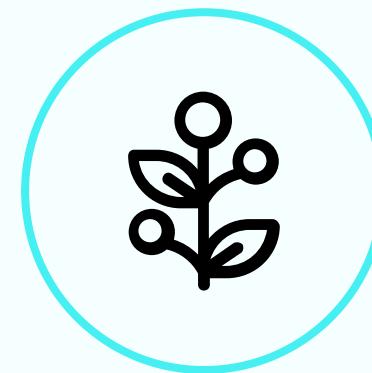


Edge genome in human pangenome graphs
[1].

Scientific Impact



Enabled later
high-coverage
genomes [2].



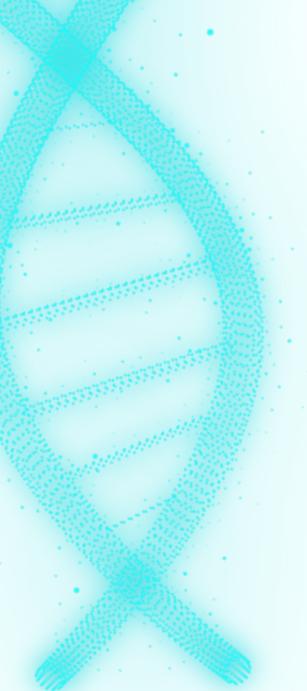
Core to Allen
Ancient DNA
Resource (AADR)
[1].



Cited >2300 times;
key to
adaptive-introgress
ion debates [1].

THANKS FOR WATCHING

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REFERENCES

- [1] Prüfer, Kay, et al. “A high-coverage Neandertal genome from Vindija Cave in Croatia.” *Science*, vol. 358, no. 6363, 3 Nov. 2017, pp. 655–658, <https://doi.org/10.1126/science.aao1887>.
- [2] Mafessoni, Fabrizio, et al. “A high-coverage Neandertal genome from Chagyrskaya Cave.” *Proceedings of the National Academy of Sciences*, vol. 117, no. 26, 16 June 2020, pp. 15132–15136, <https://doi.org/10.1073/pnas.2004944117>.
- [3] Prüfer, Kay. SNPAD: An Ancient DNA Genotype Caller, 24 Mar. 2018, <https://doi.org/10.1101/288258>.
- [4] “Map Showing the Range of Neanderthals.” Brilliant Maps, 23 Sept. 2024, brilliantmaps.com/range-of-neanderthals/.