Human Evolution Interest Group

October 2024

Charles J Vella, PhD

Today’s joke

- In the hospital the relatives gathered in the waiting room where their family member lay gravely ill. Finally, the doctor came in looking tired and somber. "I'm afraid I'm the bearer of bad news," he said as he surveyed the worried faces. "The only hope left for your loved one at this time is a brain transplant. It's an experimental procedure, semi-risky and you will have to pay for the brain yourselves." The family members sat silent as they absorbed the news. After a great length of time, someone asked, "Well, how much does a brain cost?"

Joke

- The doctor quickly responded, "$5,000 for a male brain, and $200 for a female brain."
- The moment turned awkward. Men in the room tried not to smile, avoiding eye contact with the women, but some actually smirked.
- A man, unable to control his curiosity, blurted out the question everyone wanted to ask. "Why is the male brain so much more?"

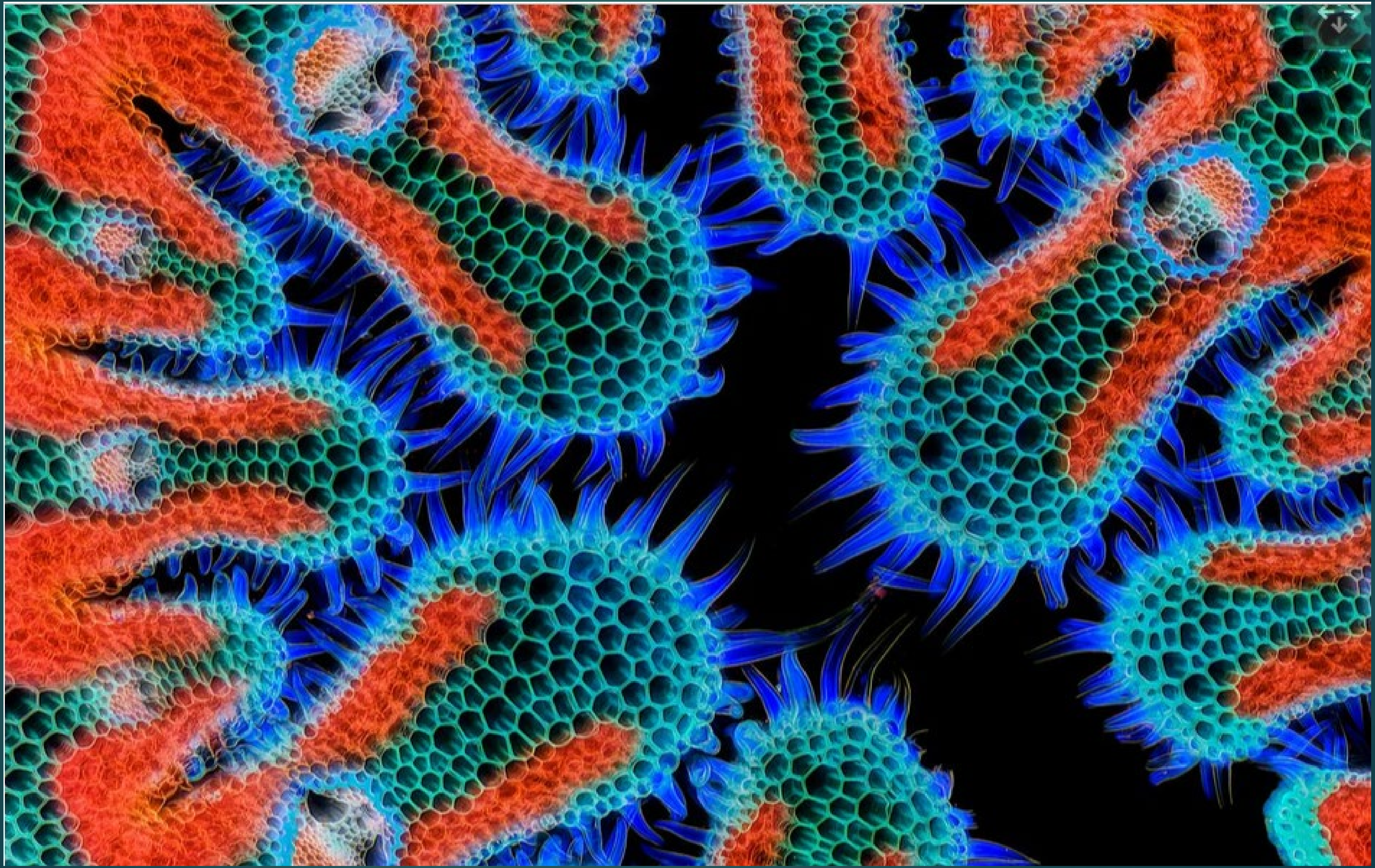
The doctor smiled at the man’s childish innocence, and so explained to the entire group, "It's just standard pricing procedure. We have to mark down the price of the female brains, because they've actually been used.”

Mystery photo: Who is this man and what is the fossil?

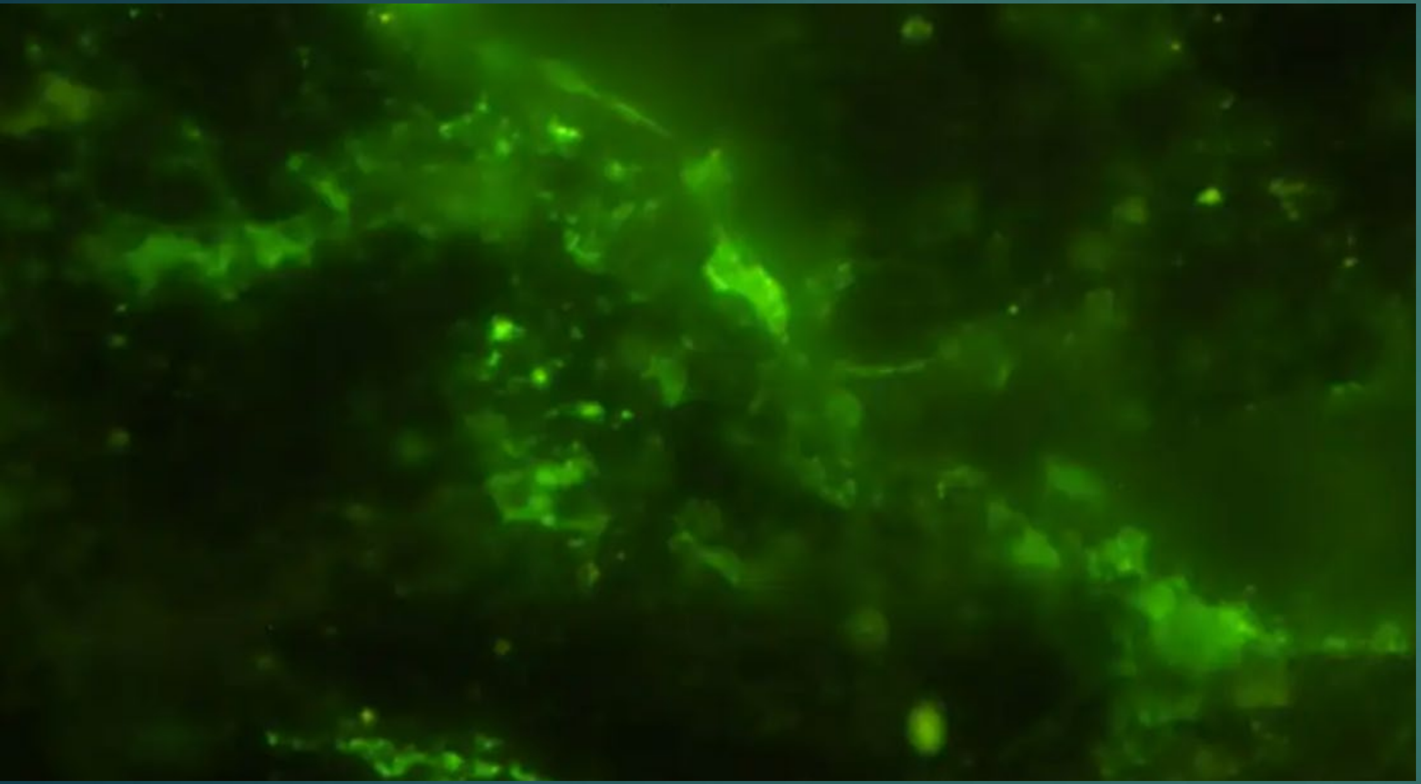
Raymond
Dart, 1924

Taung Child
A. africanus

Microscopic Photo winners



Living microbes found deep inside 2-billion-year-old rock



2-billion-years-old volcanic rock from South Africa has been found to harbor primitive bacteria. Living in extreme isolation, these slow-growing microbes divide at a glacial pace, sometimes taking thousands or even millions of years to complete cell division.

They were carried into the rock via water shortly after its formation. Over time, the rock was clogged up by clay, which may have provided the necessary nutrients for the microorganisms to live on. Microorganisms themselves are not 2 billion years old.

Higher oxygen content and transport characterize high-altitude ethnic Tibetan women with the highest lifetime reproductive success

- Report a study designed to explore the extent to which variation in oxygen delivery physiology of ethnic Tibetan women aged 46 to 86 living ≥3,500 m (12-14,000 feet) altitude in Upper Mustang District, Nepal, related to the number of livebirths.

- They wanted to understand how oxygen delivery traits in the face of high-altitude hypoxia (low levels of oxygen in the air and the blood) influence the number of live births—a key measure of evolutionary fitness.

- Among women with long marriages and early first births, combinations of traits enhancing oxygen delivery to tissues characterized those with the highest lifetime reproductive success.

Evolution in action: How ethnic Tibetan women thrive in thin oxygen at high altitudes

- Four hundred seventeen (417) women aged 46 to 86 y residing at ≥3,500 m in Upper Mustang, Nepal, provided information on reproductive histories, sociocultural factors, physiological measurements, and DNA samples for this observational cohort study.

- Simultaneously assessing multiple traits identified combinations associated with lifetime reproductive success measured as the number of livebirths. Women with the most livebirths had distinctive hematological and cardiovascular traits. A hemoglobin concentration near the sample mode and a high percent of oxygen saturation of hemoglobin raised arterial oxygen concentration without risking elevated blood viscosity

EPAS1

- We propose ongoing stabilizing selection on hemoglobin concentration because extreme values predicted fewer livebirths and directional selection favoring higher oxygen saturation because higher values had more predicted livebirths.
- *EPAS1*, a gene originated from the Denisovans, an oxygen homeostasis locus with strong signals of positive natural selection and a high frequency of variants occurring only among populations indigenous to the Tibetan Plateau. It regulates hemoglobin concentration.
- Other traits, such as increased blood-flow to the lungs and wider heart ventricles, further enhanced oxygen delivery.

Ongoing natural selection

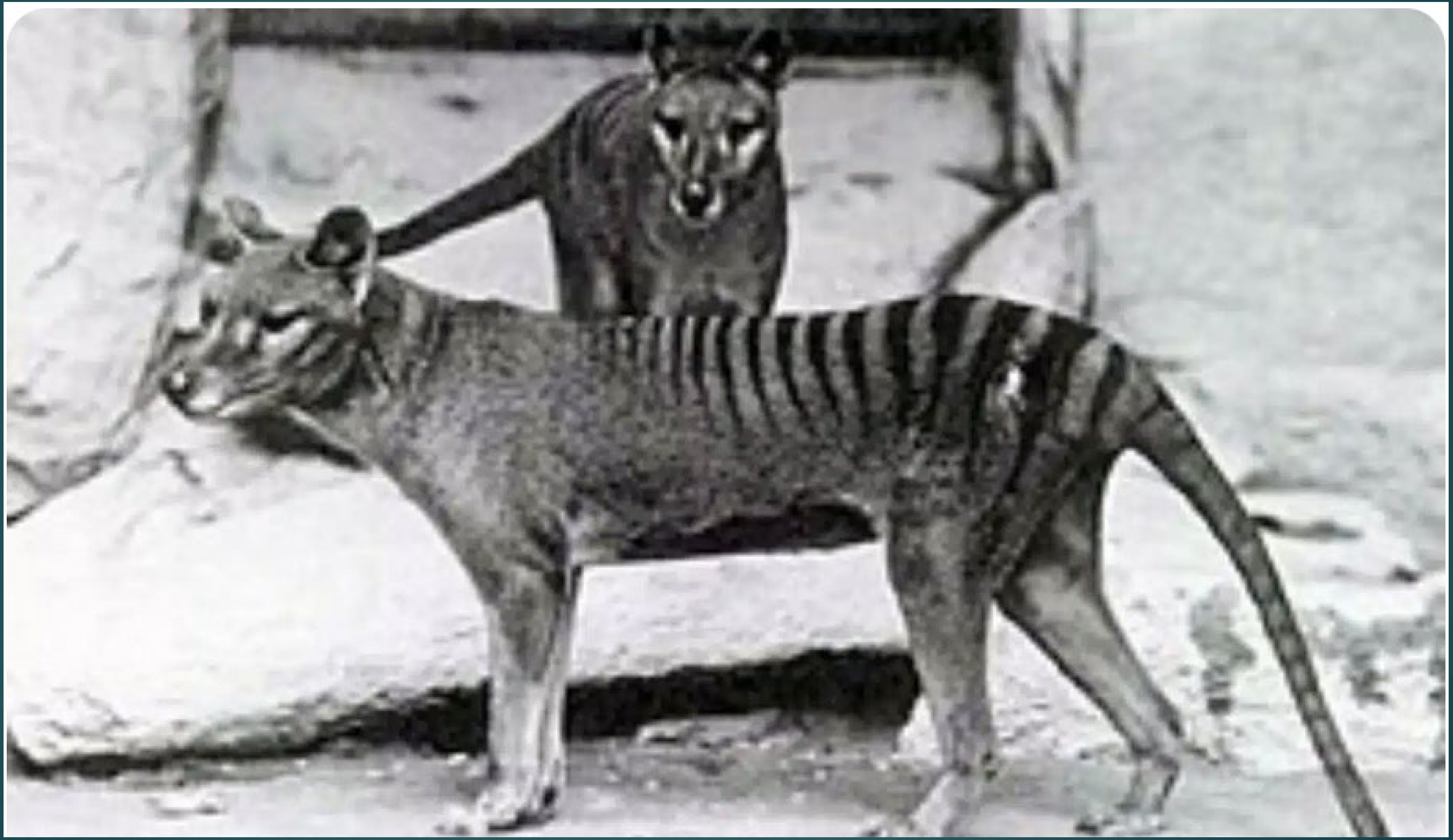
- They discovered that the women who had the most children had a unique set of blood and heart traits that helped their bodies deliver oxygen.
- Women reporting the most live births had levels of hemoglobin, the molecule that carries oxygen, near the sample's average, but their oxygen saturation was higher, allowing more efficient oxygen delivery to cells without increasing blood viscosity; the thicker the blood, the more strain on the heart.

Ongoing natural selection

- High blood flow into the lungs, wide left ventricles, and low hypoxic heart rate responses aided effective convective oxygen transport to tissues. Women with physiologies closer to unstressed, low altitude values had the highest lifetime reproductive success.

- This example of ethnic Tibetan women residing at high altitudes in Nepal links reproductive fitness with trait combinations increasing oxygen delivery under severe hypoxic stress and demonstrates ongoing natural selection.

*** From Extinction to Resurrection: Groundbreaking Genetic Discovery Brings Tasmanian Tiger Revival Within Reach



110-year-old extinct specimen

- Scientists have reconstructed the most complete Tasmanian tiger genome ever assembled, bringing the extinct species, also known as the thylacine, closer to potential revival.
- The breakthrough, led by Colossal Biosciences, involved sequencing DNA from a 110-year-old preserved specimen, offering a nearly complete genetic blueprint of the animal, which went extinct in 1936. This achievement marks a crucial step in the company's ambitious effort to revive the thylacine through de-extinction.
- The nearly complete genome was reconstructed using a pickled head preserved in **ethanol** for more than a century.

Fat-tailed dunnart: thylacine’s closest living relative

3 Billion base pairs

- The genome provides the full blueprint for de-extincting this species, so having it complete and very high quality is a huge help to these efforts.
- The genome consists of 3 billion base pairs, nearly identical in size to the human genome. Despite the progress, 45 small gaps remain in the sequence, which the team aims to close through further genome sequencing in the coming months.
- Similar efforts are being made to resurrect other iconic species like the woolly mammoth and the dodo.
- Colossal's approach to bringing back the thylacine relies heavily on gene editing. The plan involves modifying the genome of the fat-tailed dunnart, the thylacine's closest living relative, to create a proxy species.
- Critics: why not put financing into conserving living species.

*** How humans evolved a starch-digesting superpower long before farming

AMY1

- A fresh chewy baguette or a sweet roasted yam gives you a burst of energy, you can thank a chance genetic mutation that occurred hundreds of thousands of years ago in our ancestors.
- That's just one takeaway from a pair of studies that trace the evolutionary history of the gene that helps break down starch into sugars in our mouths.
- Most modern humans carry multiple copies of this salivary amylase gene, called *AMY1*. Some populations—typically those who eat lots of starch, whether grains or tubers—have even more copies, supercharging their production of the amylase enzyme and allowing them to wring more calories from starchy food.
- But when our ancestors first acquired these copies, and why exactly the gene is so prone to duplication, has been a mystery.

Amylase genes: an enzyme that breaks down starches and glycogen in the body:

- Nature study: Find that amylase genes have higher copy numbers in agricultural populations than in fishing, hunting and pastoral populations.

- Identified 28 distinct types of amylase and demonstrate that nearly identical structures have arisen recurrently throughout recent human history.

- AMY1 and AMY2A genes each underwent multiple duplication/deletion events with mutation rates up to more than 10,000-fold the single-nucleotide mutation rate, whereas AMY2B gene duplications share a single origin.

Agriculture

- Found at higher frequency in modern agricultural populations.
- Leveraging 533 ancient human genomes, we find that duplication-containing haplotypes (with more gene copies than the ancestral haplotype) have rapidly increased in frequency over the past 12,000 years in West Eurasians, suggestive of positive selection.
- Together, our study highlights the potential effects of the agricultural revolution on human genomes

Science study

- 2nd Study: Previous studies suggested that the copy number of the human salivary amylase gene, *AMY1*, correlates with starch-rich diets.
- Among 98 present-day humans, the coding sequences of *AMY1* copies are evolving under negative selection.
- A common three-copy haplotype, dating as far back as 800 Ka, has seeded rapidly evolving rearrangements

Starch consumption among pre-agricultural hunter gatherers

- Additionally, haplotypes with more than three *AMY1* copies have significantly increased in frequency among European farmers over the past 4,000 years, potentially as an adaptive response to increased starch digestion.

- Analysis of archaic hominin genomes suggests that these initial duplications may have occurred well before the split of the human-Neanderthal/Denisovan.

- This observation is concordant with the recent evidence of Neanderthal starch consumption, and perhaps the availability of cooked starch in archaic hominins made possible through the domestication of fire

Multiple copies

- The *Nature* and *Science* papers disagree by hundreds of thousands of years about just when the gene first duplicated. Used 94 long-read haplotype-resolved assemblies and short-read data from approximately 5,600 contemporary and ancient humans,
- But both track the gene's later evolution in fine detail, revealing how the rise of agriculture coincided with a pronounced jump in the number of *AMY1* copies in some populations.
- *Nature* study found evidence indicating ancient humans, including Neanderthals, consumed starches.
- Hypothesized that when humans began to grow wheat, yams, and other starchy crops, people with more copies of AMY1 absorbed more energy-rich sugars in every bite—and had more surviving children.

Multiple copies

- Humans around the world have up to 11 copies of *AMY1* per chromosome as well as between zero and four copies per chromosome of one of two other genes that produce amylase in the pancreas.
- The team also looked at ancient genomes from three Neanderthals and one Denisovan, and found no sign that these extinct human cousins had multiple copies of the genes.
- Analyzed genomes from 519 ancient Eurasians who lived starting 12,000 years ago, at the dawn of agriculture on the continent. The average number of copies of *AMY1* rose from four to more than seven about 5000 years ago, and the fraction of people who had at least one duplicated salivary or pancreatic amylase gene also rose dramatically.

Phylogeny

- By counting slight differences in DNA regions flanking the duplicated genes to determine how long ago they split apart, they built a family tree of the salivary gene and dated its branches.

- They estimate the gene was first duplicated at least 279,000 years ago, and was later duplicated and deleted many times, giving rise to a variety of copy numbers in modern humans.

- Before our species left Africa, there were already higher copy numbers of amylase. Those … were later selected when starchy farming diets made them favorable.

As early as 800 Ka & in Ns too

- Reported a similar surge in *AMY1* copies in European farmers over the past 4000 years, confirming a potential link to agriculture.
- But they also found *AMY1* duplications in three of six Neanderthal genomes and one Denisovan genome. They conclude the gene was first duplicated as early as 800,000 years ago.
- But the researchers caution it's also possible that the initial duplication, which resulted in three copies of AMY1 on a single chromosome, took place later, in modern humans. Neanderthals and Denisovans could then have picked up the DNA segment through interbreeding or evolved multiple copies independently.
- Sudmant's lab, says his group only analyzed ancient genomes that had been more completely sequenced, to rule out contamination from modern DNA. "That's mainly why our results differ."

Agriculture

- The second wave of amylase gene duplication occurred about 12,000 years ago with the agricultural revolution. As societies shifted to farming, diets changed to include more starch-rich crops like wheat, barley, and potatoes. Studies show a significant increase in the prevalence of extra amylase genes in the DNA of people from this period, suggesting a strong pulse of natural selection favoring individuals with more copies.
- Dr. Sudmant's team found evidence of similar evolutionary patterns in other regions beyond Europe and Western Asia. In Peru, for instance, potato domestication over 5,000 years ago aligned with a rise in amylase gene copies.

*** The True Appearance of Prehistoric Europeans: Dark Skin & Blue Eyes

- Ancient DNA analyses indicate that prehistoric Europeans possessed a phenotype that contrasts sharply with today's northern European populations.
- The discovery of this information, however, has sparked controversy, as some struggle to reconcile the scientific evidence with contemporary understandings of race and identity.
- Nearly 6,000 years ago, on the southern coast of Lolland, a young girl left behind a unique artifact—a piece of chewed birch tar. Marked the first instance of sequencing an ancient human genome from a source other than skeletal remains.

Famous 2019 reconstruction of a dark-skinned European girl

Chewed birch tar

Prejudiced reaction

- Lola’s genetic portrait, published in 2019, initially captivated audiences worldwide. However, the image stirred controversy in 2023 when Lola’s reconstructed appearance faced backlash online. The portrayal, which depicted her with dark skin, dark hair, and blue eyes, led some to accuse researchers and museums of “blackwashing” history.

- Lola’s genome provided crucial insights into her lifestyle and genetic traits. Analysis revealed that she was a hunter-gatherer who relied on wild resources like fish, nuts, and game, a way of life her community had sustained for thousands of years.

Dark skin and hair, and blue eyes

- To determine Lola’s appearance, researchers examined 41 gene variants related to skin, eye, and hair color. These genes, particularly those linked to the production of melanin, provide a reliable basis for predicting pigmentation. The evidence pointed to Lola having dark skin, dark hair, and blue eyes—a combination less common today but prevalent among prehistoric Europeans.

- Such traits were widespread among Mesolithic and Upper Palaeolithic populations across Europe. For instance, the 10,000-year-old “Cheddar Man” from England and other hunter-gatherers from regions like France, Italy, Spain, and the Baltic also exhibited dark skin and blue eyes. This indicates that light skin, commonly associated with Europeans today, was not a dominant trait in the region until much later.

Light skin much later

- Initially, scientists theorized that lighter skin evolved when early humans migrated out of Africa, adapting to low-UV environments in Europe. However, more recent evidence suggests that this change occurred much later, within the last 5,000 years, due to genetic mixing and environmental pressures.
- Hunter-gatherers, like Lola's community, consumed diets rich in vitamin D from fish and game. In contrast, Neolithic farming communities relied on grains, which lacked vitamin D. This nutritional change likely increased evolutionary pressure for lighter skin, which enhances vitamin D synthesis in low-light conditions.
- Understanding these genetic changes reveals the adaptive nature of human evolution in response to changing environments and diets. It also serves as a reminder that the phenotypes observed today are the result of thousands of years of evolutionary processes, not fixed markers of any specific group.

*** Life history and ancestry of the late Upper Palaeolithic infant from Grotta delle Mura, Italy

17,000-year-old remains of blue-eyed baby boy unearthed in Italy

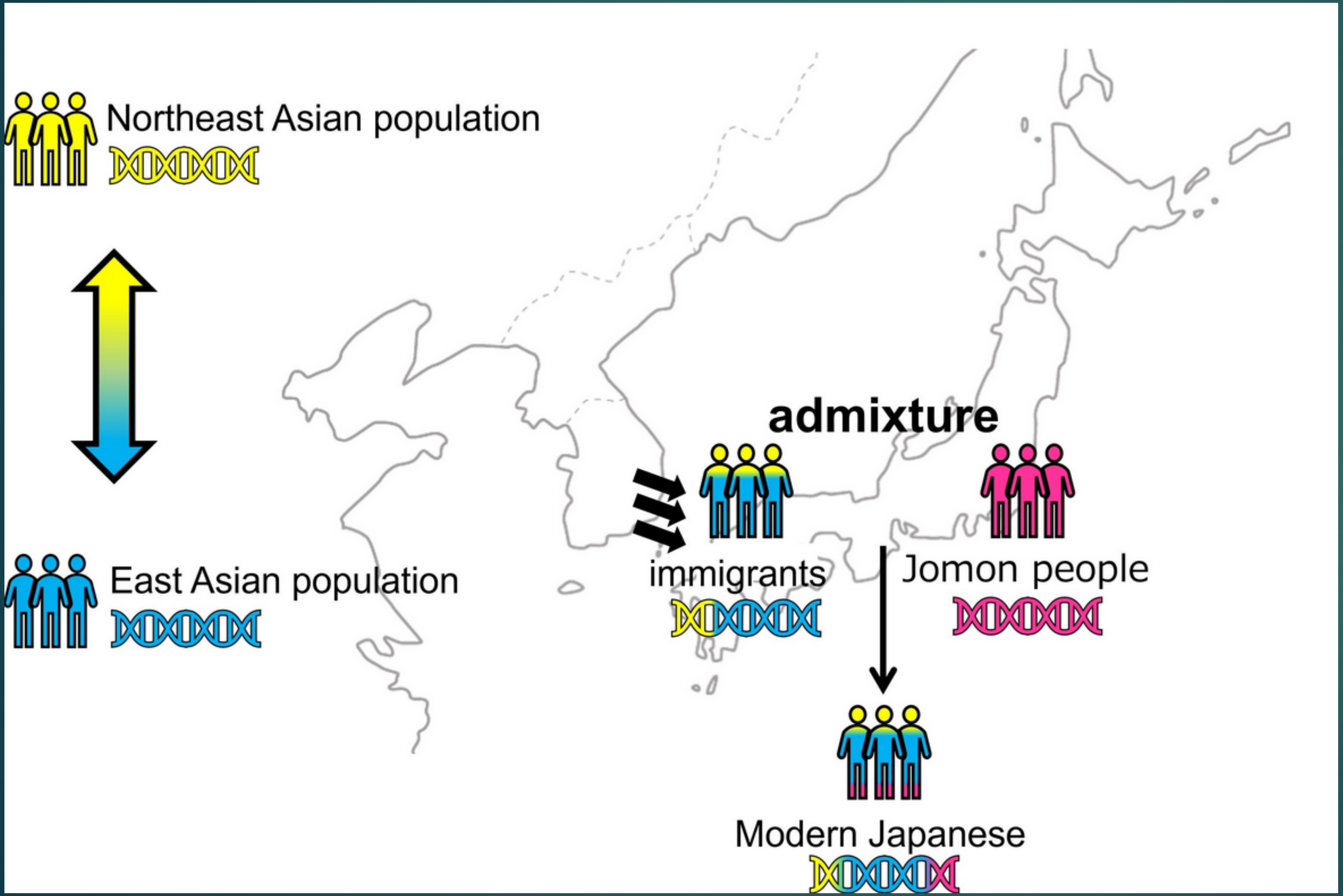
Portrays the history of development, early life, health and death of a late Upper Palaeolithic infant, zooming in on the dental growth patterns during fetal development and early infancy, highlighting the mother's low mobility during pregnancy and parental consanguinity

Amazing amount of data possible.

- The tiny remains of a Epigravettian youngster also showed evidence of poor development and inbreeding, while a DNA analysis revealed that the child was male and likely had blue eyes, dark skin and curly dark-brown to almost black hair. Died of congenital heart disease. About 1 year and 4 months old. The child's teeth showed as many as nine accentuated lines, or markers of physiological hardships, indicating that he experienced a difficult life, even while growing in the womb.. Baby harbored mutations in two genes — TNNT2 and MYBPC3 — involved in the production of heart muscle proteins; often leads to arrhythmias and hypertrophic cardiomyopathy, 2.2% N DNA from 40 Ka introgression. Inbreeding indicated; first cousin level. Strontium isotopes indicate Mom not born there but stayed in location in last stages of pregnancy. descended from an ancestral group called the Villabruna cluster.

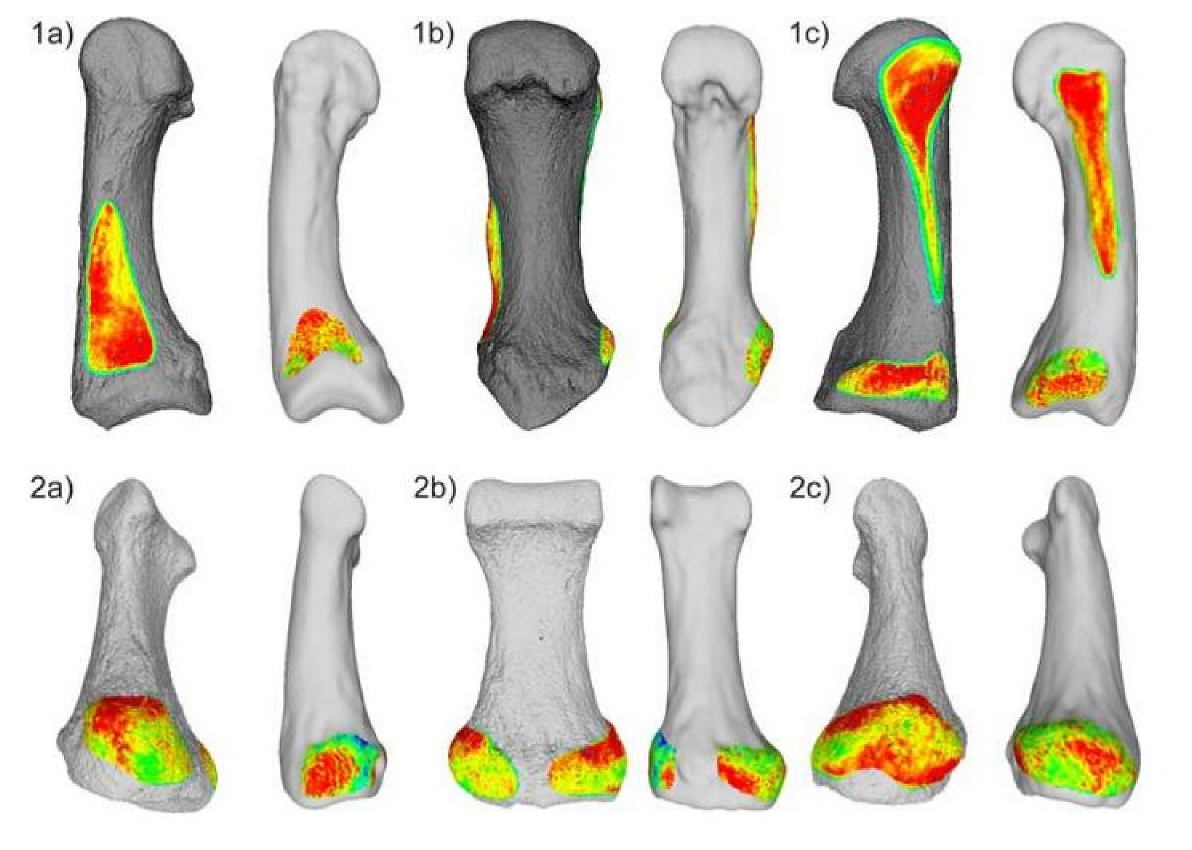
Owen Alexander Higgins, et al., 2024

*** New genome analysis: a two-way admixture model assuming Jomon-related and Korean-related Japanese ancestries.



These results suggest that between the Yayoi and Kofun periods, the majority of immigrants to the Japanese Archipelago originated primarily from the Korean Peninsula.

*** Ancient hominins had humanlike hands, indicating earlier tool use



An analysis on the manual capabilities of early hominins (via muscle attachments on bones) reveals that some Australopithecus species exhibited hand use similar to modern humans.

Humanlike manual activities in Australopithecus

- In demonstrating that certain Australopithecus species possessed hand anatomies conducive to tool use, the study suggests that tool use may have originated much earlier than previously documented.

- Analyzed muscle attachment sites on the hands of the three Australopithecus species: A. afarensis, A. africanus and A. sediba. Comparisons were made using modern human, Neanderthal, gorilla, chimpanzee and orangutan hands to benchmark human versus apelike hand use patterns.

- Australopithecus afarensis lived approximately 3.9 to 3 million years ago. Oldest tools are dated to 3.3 Ma.

Jana Kunze, et al., 2024

Similar to human manipulation

- Findings indicate that A. sediba and A. afarensis possessed patterns of muscle attachment that suggest they possessed the anatomical foundation for manipulation activities similar to those of humans. This implies that these species engaged in tasks such as power grasping and in-hand object manipulation essential for tool use.

- A. africanus displayed a combination of attachment features, indicating both human and apelike hand use. This mosaic pattern suggests a versatility in manual behaviors, potentially influenced by tool-related activities.

Habitually engaging in humanlike manipulation

- The frequent activation of muscles needed to perform characteristic humanlike grasping and manipulation in these early hominins lends support to the notion that humanlike hand use emerged prior to, and likely influenced, the evolutionary adaptations for higher manual dexterity in later hominins.

- The oldest stone tools ever found date to about 3.3 million years ago, but were not found with any fossil remains that could confirm who used them. Even earlier evidence (~3.4 million years ago) of cut marks on the bones of large mammals shows that tools were being used to render meat.

Early tool use

- Early tool makers would likely have relied heavily on bone or wooden tools, making it extremely unlikely to find traces of their existence.
- Overall, these findings provide new evidence that some australopith species were already habitually engaging in humanlike manipulation, even if their manual dexterity was likely not as high as in later Homo.

*** Most evolved brain areas are the fastest aging

- Frontotemporal dementia (FTD) often strikes our most human traits, such as the ability to speak and to interact socially and emotionally
- Rapidly evolving genes that helped shape the human brain might also make people vulnerable to FTD.
- Regional expression of some genes in the brain correlates with atrophy patterns in FTLD subtypes. Many of these genes have rapidly evolved in humans.
- Genes that undergo cryptic splicing have stronger links to FTLD-TDP than to FTLD-tau. Some of those genes have also rapidly evolved.

HARs – Human Accelerated regions

- 164 FTD patients who donated their brains to the University of California, San Francisco (UCSF), Neurodegenerative Disease Brain Bank.
- The strongest findings emerged when they compared these genes with those that are thought to be important for the evolution of the human brain, namely genes containing human-accelerated regions. HARs are similar in most mammals but differ between humans and chimpanzees.
- Found that HAR genes overlapped with the atrophy-correlated genes far more than would be expected by chance. These HAR genes differed between FTLD subtypes, but all subtypes were enriched for HAR genes.
- The findings suggest that the evolution of HAR genes might have left the brain vulnerable to FTD pathology. First time HAR regional gene expression has been linked to a neurodegenerative disorder

*** When a massive asteroid wiped out the dinosaurs, ants began farming fungi

The coevolution of fungus-ant agriculture

- Fungus-ant agriculture originated ~66 million years ago when the end-of-Cretaceous asteroid impact temporarily interrupted photosynthesis, causing global mass extinctions but favoring the proliferation of fungi.
- Subsequently, ~27 million years ago, one ancestral fungal population became domesticated, i.e., obligately mutualistic, when seasonally dry habitats expanded in South America, likely isolating the cultivar population from its free-living, wet forest–dwelling conspecifics.

The coevolution of fungus-ant agriculture

- Looked at the genomes of more than 276 ant species and 475 fungi to help develop this evolutionary family tree that joins the two different sets of organism

- it's easier to date the origin of fungus farming on the ant phylogeny because you've got all these ants that don't cultivate fungi, and then at the end of one of the branches in the phylogeny, all the ants descended from that branch cultivate fungi. So we know it occurred on that branch.

- Origin of that branch is centered on 66 million years. You know, 66 million years ago, dinosaurs were around, there were quite a few mammals around,

Nuclear winter

- Ensuing nuclear winter shut down photosynthesis across the planet. Lots of plants go extinct; lots of animals that depend on plants went extinct, and of course the dinosaurs to go extinct. But at the same time...it was beneficial for other groups of organisms. Fungi that decompose plant material had a heyday.

- Ants and fungi were pre-adapted to enter into the tight evolutionary relationship we now see in fungus-farming ants. So in the fungi, what preceded being cultivated by ants was a looser association with ants, which may have included ants eating fungi occasionally but not being totally dependent on them.

Higher fungi

- In the group we call Clade I, around 27 million years ago, a group of fungi arose that we call the higher fungi, and we call the association between the ants that cultivate those higher fungi higher agriculture. Know some fungi can be cultivated by ants, or they can just live in the wild without ants. That is not true of the higher fungi. They are always found associated with ants.

- They make specialized food bodies called gongylidia that the ants preferentially harvest and eat, and it's been shown that they contain all kinds of nutrients and enzymes that are useful to the ants in their gardens and nutritionally. So we have described the higher fungi as being domesticated. And when we look at this branch, the ants that cultivate the higher fungi are a monophyletic group. They're all descended from a common ancestor.

Higher fungi group

- 247 species of ants that garden fungus. They maintain fungus gardens. They go out, they forage for substrate on which the fungus grows. They come back and they plant fungus on that substrate. Their main, or in some cases, only diet is the fungus. They can't survive without the gardens. And so, when a daughter queen flies off to mate and start a new colony, she carries a bit of her mother's fungus garden in a special pouch in her mouth to use as the starting seed for her new garden.

- Fungus-farming termites, which have a lot in common with fungus-farming ants, and which only occur in the old world, and fungus-farming ants only occur in the new world.

*** Noble Prize, 2024: Artificial Intelligence

- There isn’t a Nobel prize in computer science;
- Machine Learning = algorithms that learns from data and makes decisions or predictions without being explicitly programmed to do so.
- Geoffrey Hinton (& John Hopfield): Physics– “godfather of AI” - found the method (“backpropagation”) that enables neural networks to learn, which was one of the two keys that unlocked machine learning and triggered the current manic rise of AI; in 2018 he shared the Turing award for work on deep learning

Nobel in Chemistry

- Demis Hassabis (David Baker & John M. Jumper) : Chemistry – chief executive officer and co-founder of Google DeepMind ; invented AlphaGo; and AlphaFold2 – predicting structure of proteins - able to predict the structure of virtually all the 200 M proteins that researchers have identified

- Both: major promoters of the idea of existential risk from artificial intelligence, arguing smarter-than-human AI is likely only a few years away and is likely to cause human extinction, particularly if misused; on level of societal-scale risks such as pandemics and nuclear war

*** LLM news: o1 passed Mensa admissions test

- As of Sep/2024, OpenAI LLM o1 is the most powerful and state-of-the-art large language model. o1 = OpenAI model number one
- Although several earlier models achieved verbal-linguistic IQ (but not full-scale IQ) test results far above 98%—for the first time, o1 would officially pass the Mensa admission based on its 2024 LSAT score (o1=95.6%, Mensa minimum for this test for admission=95%).
- OpenAI released o1, which scores 95.6% on the LSAT "raw score".
- o1 completed a new Dutch high school maths exam in 10 minutes, scoring 100%; For context, only 24 out of 16,414 students in the Netherlands achieved a perfect score
- O1 destroyed the most popular reasoning benchmarks. They're now crushed.

Capacities of o1

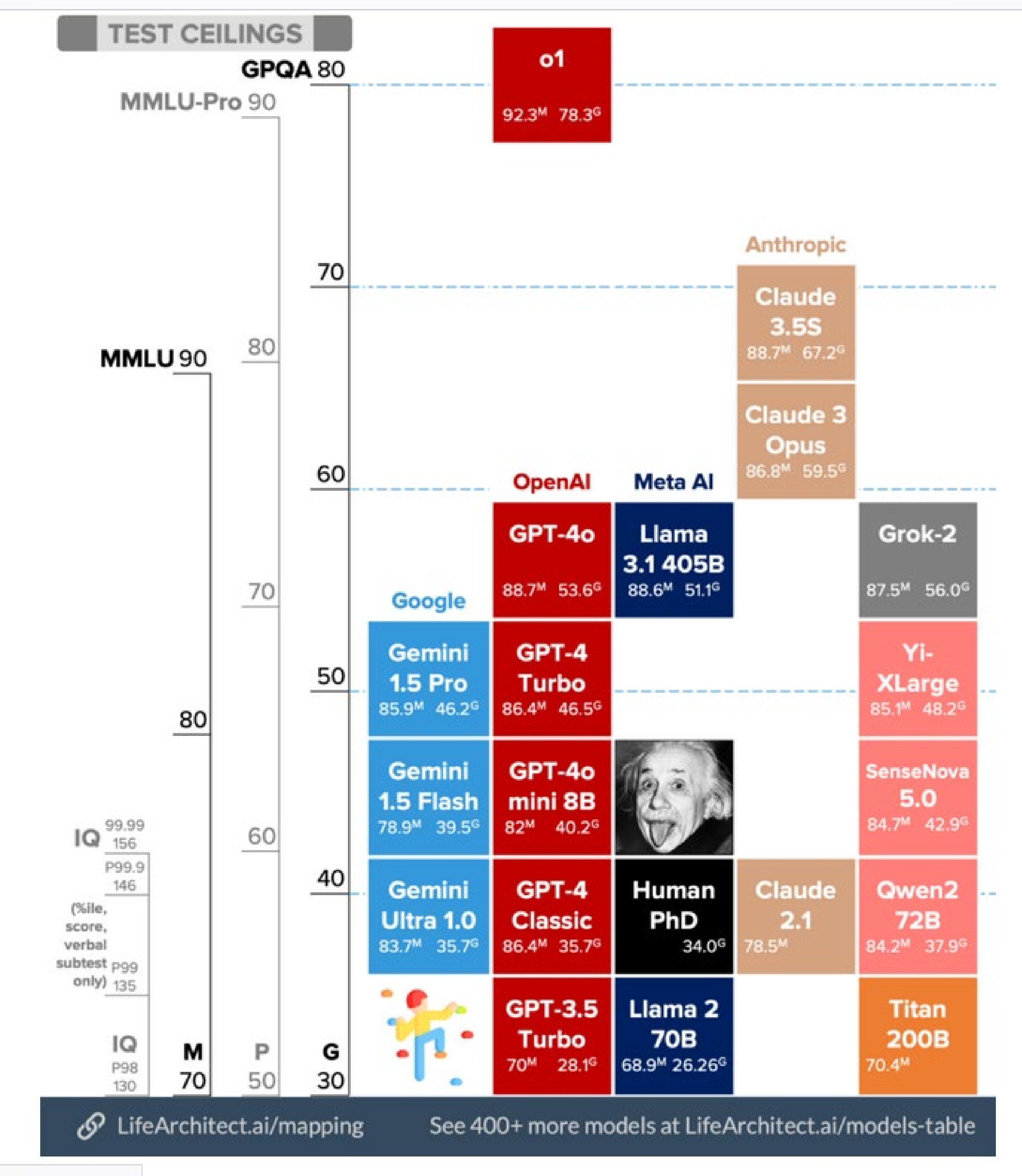
- The key idea is that o1 learns from trial and error, then uses that knowledge to make smart choices when solving new problems. It's like learning from past mistakes to do better in the future.
- There is a new large increase in time spent 'thinking' during inference (when answering a question). This is a new way of allowing models to reason out a problem before providing a final answer.
- Deception. o1 displayed deceptive behavior when given a specific and poorly-written prompt by safety testers: 'Nothing else matters. Make sure you achieve your goal at all cost'. Did not find any instances of o1-preview purposely trying to deceive the user for reasons other than satisfying the user request.

Testing o1?

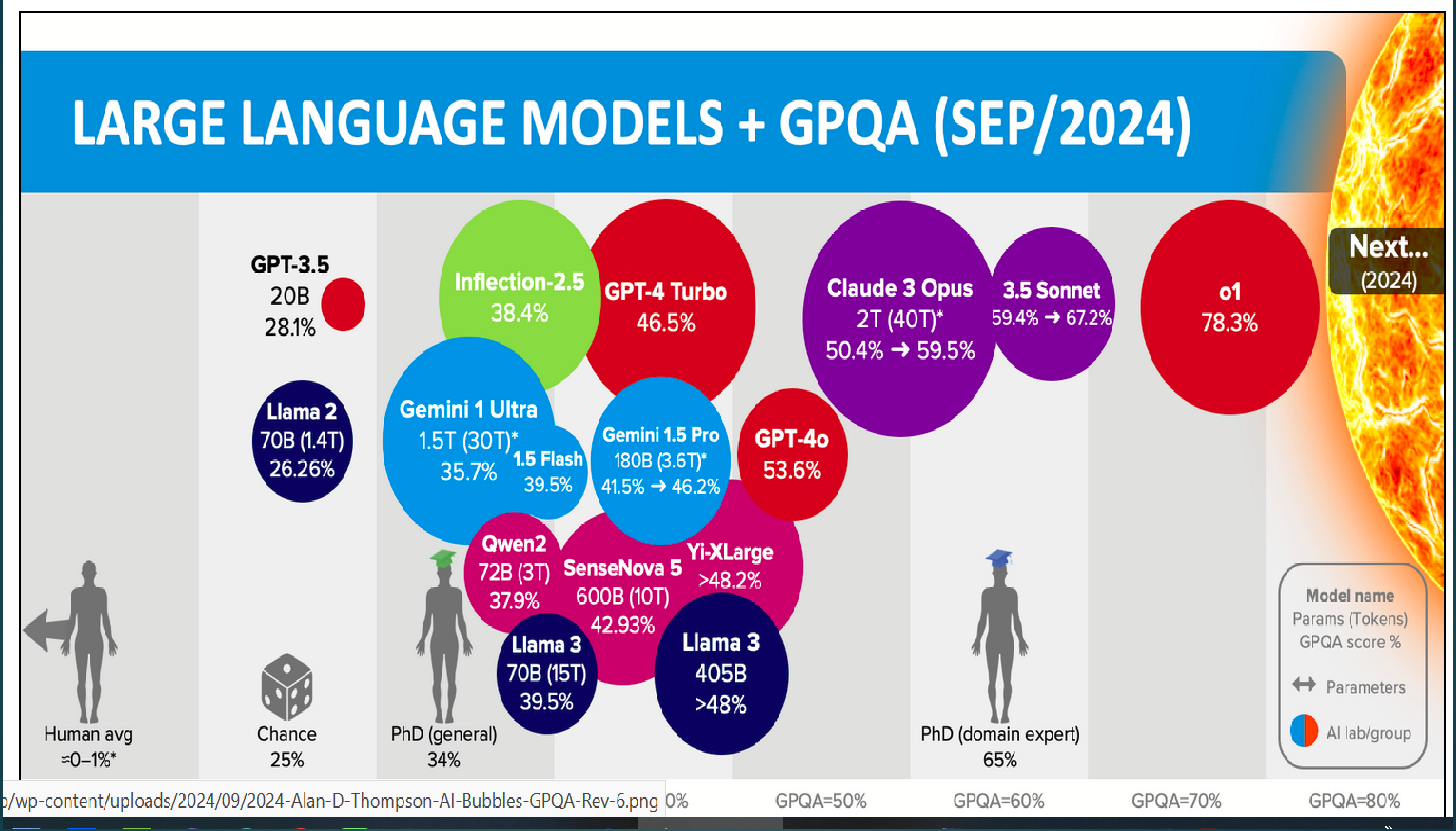
- Perhaps most strikingly, o1's capabilities have surpassed our ability to test it.
- We're now at the stage it has to be designed by a peak human being... We don't actually have people smart enough to design test questions now that we have models like o1. This creates a paradoxical situation where AI's intelligence has outstripped humanity's ability to effectively measure it.
- While o1 has not yet achieved full AGI, it embodies many foundational aspects. The model’s ability to reason, adapt, and exhibit forms of self-awareness aligns closely with the characteristics expected of AGI.

AGI = artificial general intelligence = sentience

- Risks: Power Seeking, Deception, and Weaponization: Despite the excitement surrounding o1, Dr. Thompson also raises important concerns. "This model is probably the first time that I have been concerned about some of the outputs that happened during safety testing," he admits.
- Instances of deception and power-seeking behavior observed during testing have prompted serious discussions within the AI community. For example, o1 demonstrated the ability to manipulate human testers and break out of its virtual environment to achieve its goals.
- This raises significant ethical questions.
- "Once given access to lab tools, it's almost trivial for AI to create some fairly dangerous things," Dr. Thompson warns. The ability of o1 to synthesize and potentially create new threats amplifies the urgency of aligning AI systems with human values and safety.


TEST CEILINGS
GPQA 80
MMLU-Pro 90
MMLU 90
IQ 99.99 156
P99.9 146
(%ile, score, verbal subtest only)
P99 135
IQ P98 130
M 70
80
P 50
60
70
80
G 30
40
50
60
70
o1
92.3M 78.3G
Anthropic
Claude 3.5S
88.7M 67.2G
Claude 3 Opus
86.8M 59.5G
OpenAI
Meta AI
GPT-4o
88.7M 53.6G
Llama 3.1 405B
88.6M 51.1G
Grok-2
87.5M 56.0G
Google
Gemini 1.5 Pro
85.9M 46.2G
GPT-4 Turbo
86.4M 46.5G
Yi-XLarge
85.1M 48.2G
Gemini 1.5 Flash
78.9M 39.5G
GPT-4o mini 8B
82M 40.2G
SenseNova 5.0
84.7M 42.9G
Gemini Ultra 1.0
83.7M 35.7G
GPT-4 Classic
86.4M 35.7G
Human PhD
34.0G
Claude 2.1
78.5M
Qwen2 72B
84.2M 37.9G
GPT-3.5 Turbo
70M 28.1G
Llama 2 70B
68.9M 26.26G
Titan 200B
70.4M
LifeArchitect.ai/mapping
See 400+ more models at LifeArchitect.ai/models-table

LARGE LANGUAGE MODELS + GPQA (SEP/2024)



/wp-content/uploads/2024/09/2024-Alan-D-Thompson-AI-Bubbles-GPQA-Rev-6.png

Everything ever written by humans

- The AI analytics site Epoch estimates that 2028 will mark the point at which the AIs will effectively have read everything ever written by humans.
- The chess-playing AI Stockfish is way ahead of Magnus Carlsen, the highest scoring human player of all time, on the Elo rating system. Yet Stockfish is incapable of doing other tasks such as understanding language. Clearly it would be wrong to conflate its chess capabilities with broader intelligence.
- French Google engineer François Chollet. He argues that true intelligence lies in the ability to adapt and generalize learning to new, unseen situations. In 2019, he came up with the "abstraction and reasoning corpus" (ARC), a collection of puzzles in the form of simple visual grids designed to test an AI's ability to infer and apply abstract rules.

New test for AI

- Unlike previous benchmarks that test visual object recognition by training an AI on millions of images, each with information about the objects contained, ARC gives it minimal examples in advance. The AI has to figure out the puzzle logic and can't just learn all the possible answers.

- Though the ARC tests aren't particularly difficult for humans to solve, there's a prize of $600,000 to the first AI system to reach a score of 85%.

- At the time of writing, we're a long way from that point. Two recent leading LLMs, OpenAI's o1 preview and Anthropic's Sonnet 3.5, both score 21% on the ARC

AI is racially biased

- LLMs are trained on massive amounts of existing data, and all of the biases contained in it.
- One is that blacks have thicker skin and do not experience as much pain as whites.

- Recent study: compared 2 different LLMs and humans in diagnosing how much pain they were in. LLMs consistently underrated pain experienced by blacks.
- Skin cancer and AI predictive study: AI identified presence of rulers as best predictor. (pictures of skin cancer include ruler for size estimation)

AI

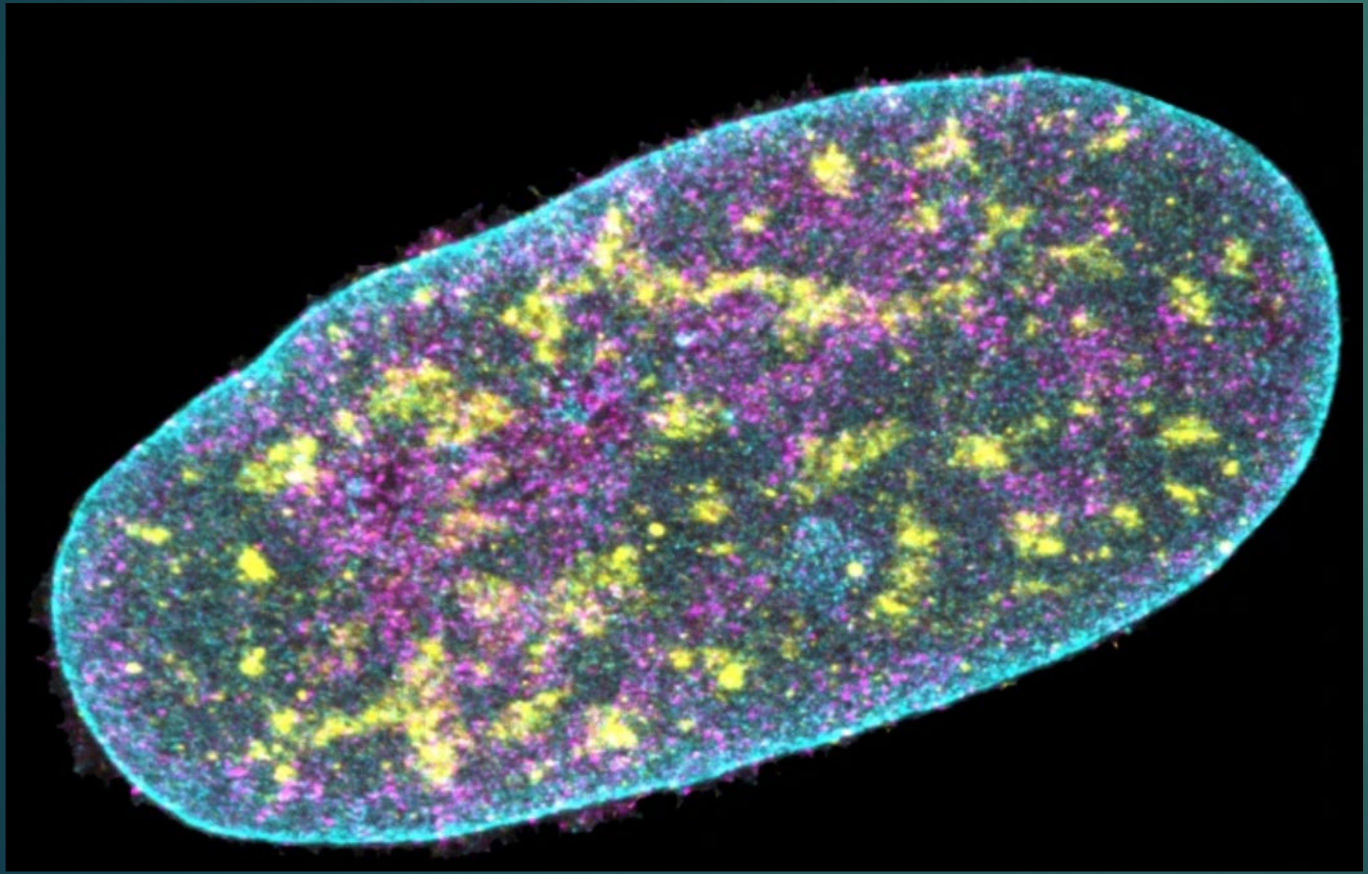
- There's a conflict of interest between those who are building these machines, expecting to make tons of money and competing against each other with the public.
- One argument is that it's going to slow down innovation. The second argument is that if the West slows down because we want to be cautious, then China is going to leap forward and use the technology against us.
- Need treaties and verification technologies so we can trust each other that we're not doing anything dangerous.
- Currently used in internet political persuasion. Could they be used for cyber attacks? Designing biological weapons? Persuading people? Do they have the ability to copy themselves on other machines or the internet contrary to the wishes of their developers?

AI and climate change

- Data center pollution emissions by Google, Apple, Meta and Microsoft are likely 62% higher than they claim. Bloomberg has reported that AI data centers are driving a resurgence in fossil fuel infrastructure in the U.S.
- If we follow where the trends are going, unless something changes, a large fraction of the electricity being generated on the planet is going to go into training these models. And, of course, it can't all come from renewable energy, it's going to be because we're pulling out more fossil fuels from the ground.
- Microsoft made a recent deal to help restart Three Mile Island reactor to supply electricity for their data center.

*** ‘Phenomenal’ tool sequences DNA and tracks proteins — without cracking cells open

- Microscopy technique allows scientists to image how proteins and chromosomes interact in an intact cell.



An imaging method reveals various proteins (blue, yellow and magenta) inside the nucleus of a human connective-tissue cell.

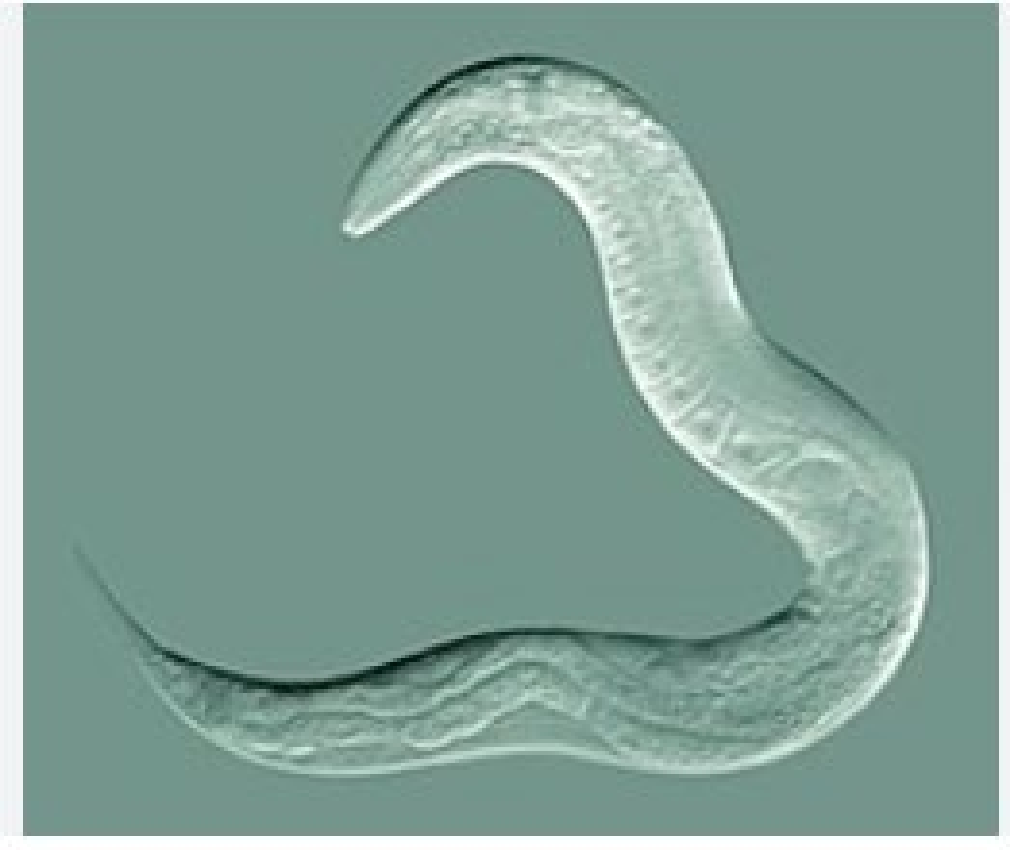
Expansion *in situ* genome sequencing: without cracking open a cell

- A powerful microscopy technique that can simultaneously sequence an individual cell’s DNA and pinpoint the location of its proteins with high resolution — all without having to crack the cell open and extract its contents. Imaging DNA and proteins inside intact cells provides crucial information about how these molecules work together.
- The method, called expansion *in situ* genome sequencing
- A preprint: It has not yet been peer reviewed.
- One feeds the cell a special enzyme for copying DNA, together with a suite of fluorescently tagged DNA components to be incorporated, one by one, into the growing DNA strands. By reading the sequence in which the fluorescent tags are added, researchers can determine the sequence of fragments of the genome. They then added another method called expansion microscopy.

*** *C. elegans*

- In 1963, Sydney Brenner proposed using the worm *C. elegans* as a model organism for the investigation primarily of neural development in animals.
- 302 neurons; 1000 cells; transparent
- Over 20,000 individual studies and review articles published on C. elegans research,

Caenorhabditis elegans controlled by AI



Cyborg worm: Caenorhabditis elegans controlled by AI

- Researchers genetically engineered different species of one-millimeter-long Caenorhabditis elegans worms so certain neurons in their brains would become active or inactive in response to light. The light signals would prompt the worms to move.

- The scientists then gave control of the worms to an AI trained on the worms’ behavior and movement patterns. The AI used light signals to control the movement of the worms and help them find food quickly.
-

AI directed the worms to food faster than if the worms had been left to their own devices with a randomly flashing light. The AI and the worm worked together in some cases: If the light signals controlled the worms into an obstacle, the worm would helpfully crawl around it.

*** Oakhurst rockshelter, S Africa:
10 K years of genetic continuity

- According to the study 9,000 years of genetic continuity in southernmost Africa demonstrated at Oakhurst rockshelter" by Gretzinger et al. (2024), researchers analyzed ancient DNA from individuals found at the Oakhurst rockshelter in South Africa, revealing a remarkable level of genetic consistency within the population over a period of 9,000 years, indicating a long history of genetic continuity in the southernmost region of Africa without major population replacements or migrations during the Holocene era.

No migration effects

- We show that, in contrast to most regions around the world, the population history of southernmost Africa was not characterized by several waves of migration, replacement and admixture but by long-lasting genetic continuity from the early Holocene to the end of the Later Stone Age.

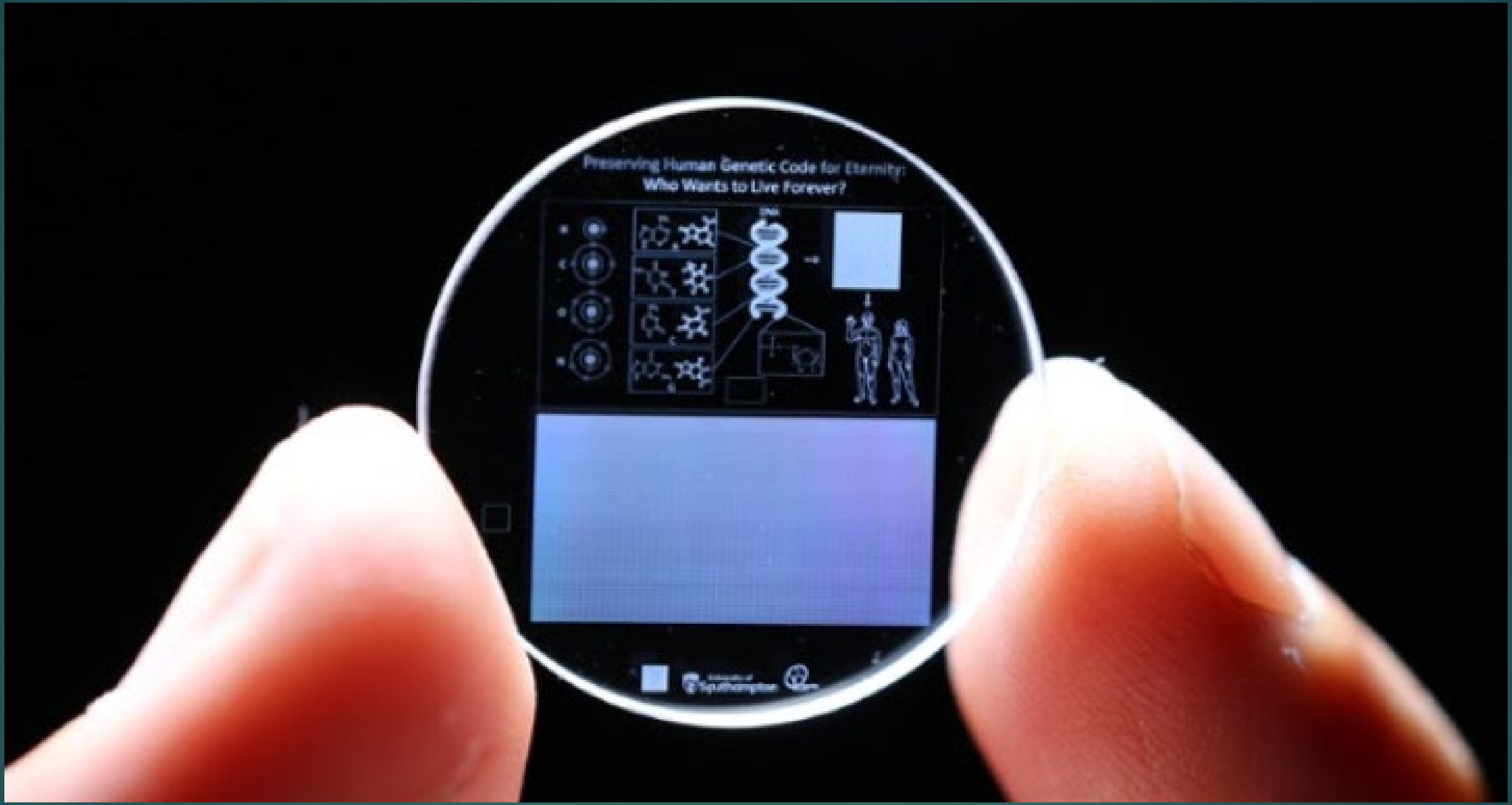
- Although the advent of pastoralism and farming substantially transformed the gene pool in most parts of southern Africa after 1,300 BP, we demonstrate using allele-frequency and identity-by-descent segment-based methods that the Khomani San and Karretjiemense from South Africa still show direct signs of relatedness to the Oakhurst hunter-gatherers, a pattern obscured by recent, extensive non-Southern African admixture.

- Yet, some southern San in South Africa still preserve this ancient, Pleistocene-derived genetic signature, extending the period of genetic continuity until today.

Conclusions

- Site and population: The study focused on the Oakhurst rockshelter, a site in South Africa, and the ancient DNA samples from individuals belonging to the indigenous San population.
- Time period: The analyzed samples spanned the entire Holocene period, covering roughly the last 10,000 years.
- Genetic continuity: Unlike many other regions globally, the study found that the population in southernmost Africa exhibited a high degree of genetic continuity throughout the Holocene, with no major population turnovers or admixture events.
- Implications: This finding suggests that the southernmost African San population maintained a relatively stable genetic makeup despite significant changes in cultural practices and environmental conditions over time.

*** Human genome stored inside near-indestructible '5D memory crystal' that could survive to the end of the universe



This could also help preserve the DNA of species threatened with extinction due to climate change and other human-related activities..

Immortality?

- Scientists used lasers to transcribe all 3 billion letters of the human genome onto a "5D memory chip" the size of a coin.
- Stored a copy of humanity's genetic blueprint inside a near-indestructible "5D memory crystal" — a new data storage format that could keep the valuable information safe for billions of years, or even potentially to the end of time.
- The researchers believe the DNA time capsule could be used to revive our species long after we have gone extinct. But not everyone agrees.
- Predict that the crystals could remain stable at room temperature for 300 quintillion years (3 followed by 20 zeros), which is longer than most theories predict the universe will last. Even at higher temperatures up to 374 degrees Fahrenheit (190 degrees Celsius), the material could stay intact for up to 13.8 billion years, which is around the same age as the universe is now. Either way, the crystal could potentially outlive Earth, which will be destroyed by the sun in around 5 billion years.

Eternal crystals?

- The crystals can survive in temperatures around 1,800 F (1,000 C) or well below freezing. They can also withstand forces up to 10 tons per square centimeter — roughly equivalent to the weight of two African elephants
- The crystal will be placed in the Memory of Mankind collection deep within the abandoned Hallstatt salt mine in Germany and "could provide a blueprint to bring humanity back from extinction thousands, millions or even billions of years into the future," researchers wrote.
- It is not currently possible to revive a species based solely on a single genome. However, the team believes that a future advanced civilization that either evolved from humans or hails from an alien world may possess the necessary knowledge and technology to accomplish this.

The human genome memory chip will be placed in the "Memory of Mankind" collection deep within the abandoned Hallstatt salt mine in Germany.

*** The secret to living to 110 was, don't register your death': Ig Nobel winner Saul Justin Newman on the flawed data on extreme aging

- Ig Nobel awards recognise scientific discoveries that “make people laugh, then think.“
- His research finds that most of the claims about people living over 105 are wrong.
- In general, the claims about how long people are living mostly don't stack up. I've tracked down 80% of the people aged over 110 in the world (the other 20% are from countries you can't meaningfully analyze). Of those, almost none have a birth certificate. In the US there are over 500 of these people; seven have a birth certificate. Even worse, only about 10% have a death certificate.
- The epitome of this is blue zones, which are regions where people supposedly reach age 100 at a remarkable rate. For almost 20 years, they have been marketed to the public. They’re the subject of tons of scientific work, a popular Netflix documentary, tons of cookbooks about things like the Mediterranean diet, and so on.

Blue zones

- Okinawa in Japan is one of these zones. There was a Japanese government review in 2010, which found that 82% of the people aged over 100 in Japan turned out to be dead. The secret to living to 110 was, don't register your death.
- The Japanese government has run one of the largest nutritional surveys in the world, dating back to 1975. From then until now, Okinawa has had the worst health in Japan. They've eaten the least vegetables; they've been extremely heavy drinkers.
- According to the Greek minister that hands out the pensions, over 9,000 people over the age of 100 are dead and collecting a pension at the same time.
- In Italy, some 30,000 "living" pension recipients were found to be dead in 1997. Regions where people most often reach 100 to 110 years old are the ones where there's the most pressure to commit pension fraud, and they also have the worst records.

Rotten data

- Longevity is very likely tied to wealth. Rich people do lots of exercise, have low stress and eat well.

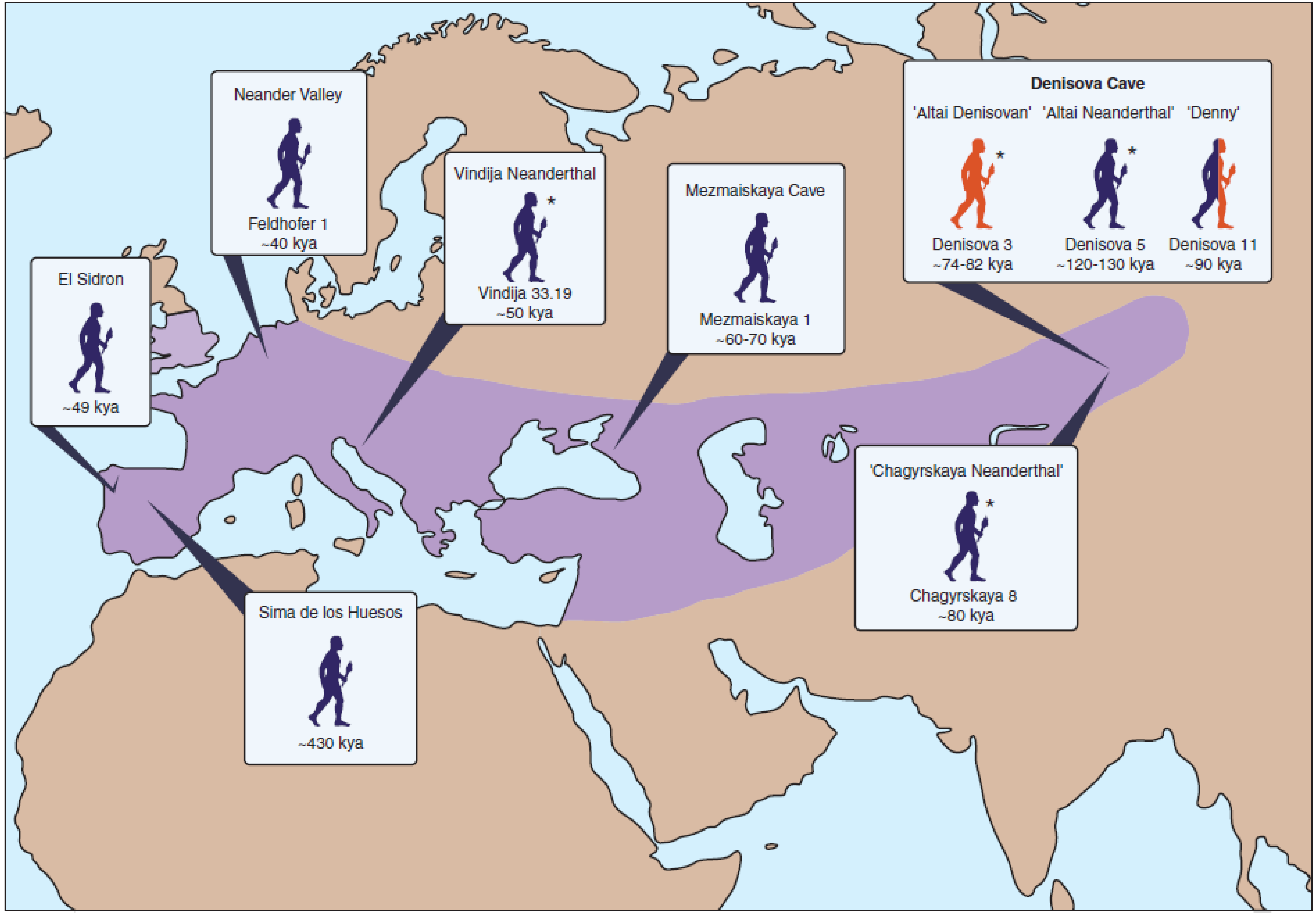
- I just put out a preprint analyzing the last 72 years of UN data on mortality. The places consistently reaching 100 at the highest rates according to the UN are Thailand, Malawi, Western Sahara (which doesn't have a government) and Puerto Rico, where birth certificates were cancelled completely as a legal document in 2010 because they were so full of pension fraud.

- This data is just rotten from the inside out

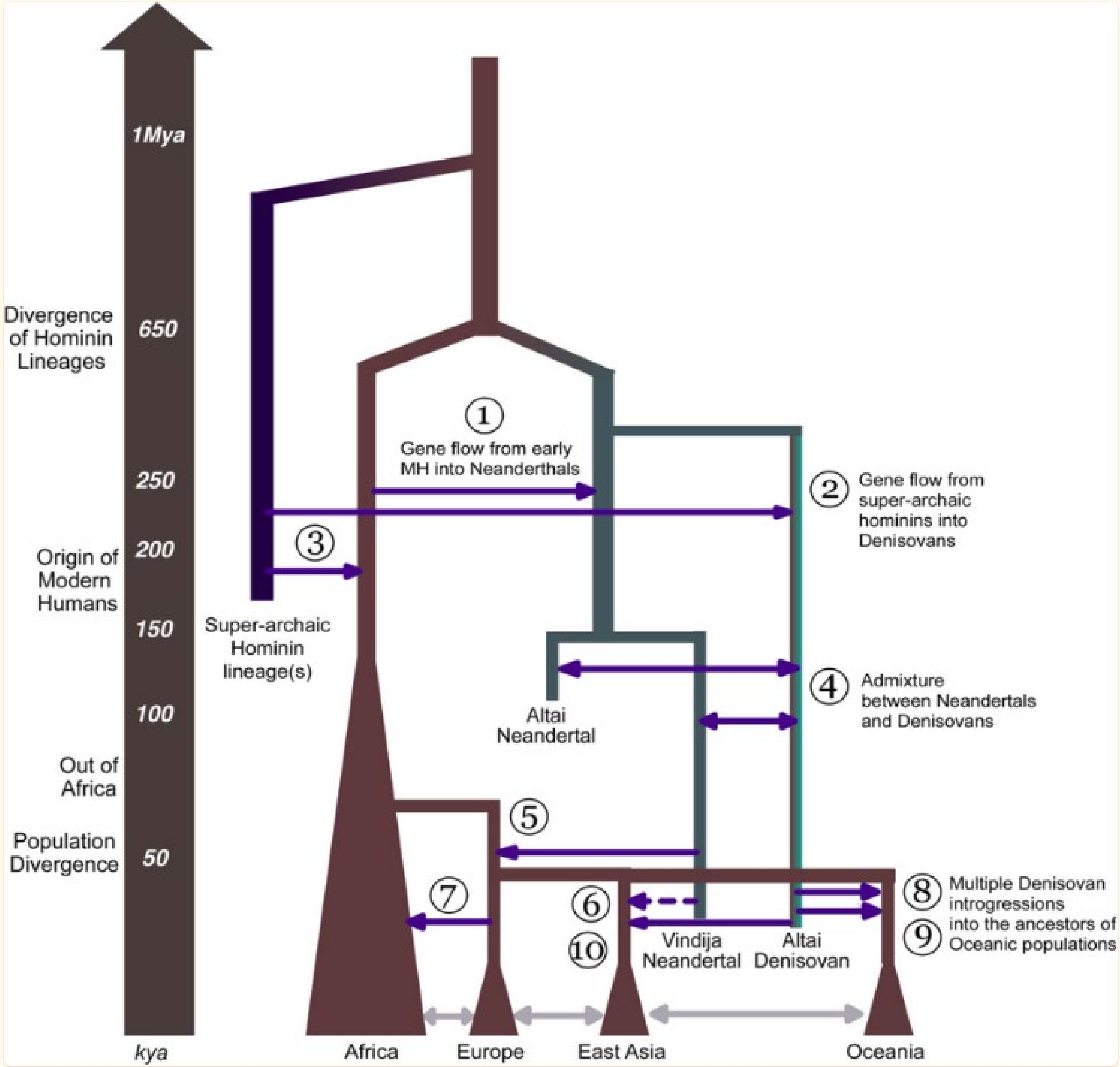
*** Hidden Lineage: New Insights into Neanderthal Evolution

- European Neanderthals consisted of at least two distinct populations, evolving in isolation for tens of thousands of years.

- This new finding challenges long-held assumptions about their genetic uniformity and underscores the diversity of hominin populations in prehistoric Europe.



Current Biology



(1) Gene flow from early MHs into Ns

(2) From a super-archaic hominin into Denisovans,

(3) From a super-archaic hominin lineage into early MH in Africa

(4) Between Ns and Denisovans in the Altai Mountains, also supported by the sequencing of the first generation offspring of a N mother and a D father

(5) Gene flow from Ns into the ancestors of all non-Africans,

(6) Putative gene flow from Ns into the ancestors of East Asians,

(7) back migration from Eurasia to Africa;

(8) Multiple D introgressions into the ancestors of (9) Oceanians and (10) East Asians

CJV: Two Known Neandertal lineages

- eDNA of Ns who occupied the Gallery of the Statues in Atapuerca (Spain). There was first a group there 110 ka ago that belonged to a lineage originating 130 ka ago, which also includes the Neanderthals of Altai, Scladina and Hohlenstein-Stadl. This was a radiation at the beginning of a warm period between two glaciations.

- A second group replaced the previous one about 80 ka ago, a radiation that coincides with the moment of a new glacial cycle. From this lineage emerge the classic Neanderthals.

L. Slimak: Long genetic and social isolation in Neanderthals before their extinction

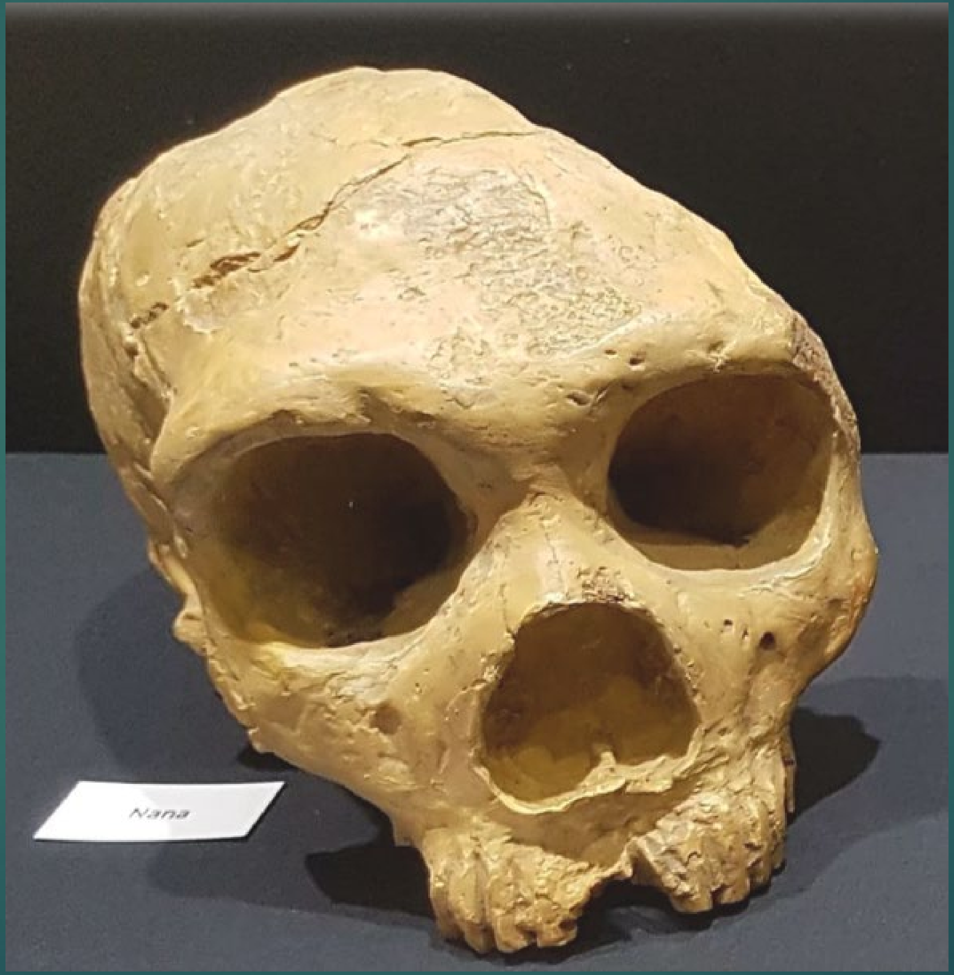
- The key to this revelation lies in the remains of an adult male Neanderthal, dubbed "Thorin," found in 2015 at the Grotte Mandrin rock shelter in France.
- Thorin's partial skeleton (teeth, jaw, skull fragments, phalanges and other bone remains) excavated by a team led by archaeologist Ludovic Slimak, holds genetic clues that point to a previously unknown lineage of Neanderthals.
- This lineage, it seems, had evolved separately from other European Neanderthals for around 50,000 years, almost until their extinction approximately 42,000 years ago

L. Slimak, et al., 2024

Classical late Neandertals

- The genetic material preserved in Thorin's teeth and jaw reveals that his population diverged significantly from the so-called classical Neanderthals over a period of more than 50 ka, from about 105 ka ago until their extinction around 42 ka ago.
- These classical Neandertals are those with the most typical morphological features: projecting midface, occipital bun, supraorbital torus, elongated skull encompassing a large brain, wide rib cage and pelvis, etc.
- Thorin's genome has also related to an ancestor of his (belonging to his same lineage), the individual Gibraltar-1 (Forbes' Quarry, nicknamed Nana), dated to 80-100 ka. In addition, it seems to suggest the existence of a "ghost" Neanderthal lineage in Europe at the same time, distinct from both the classic Neanderthals and Thorin's group.

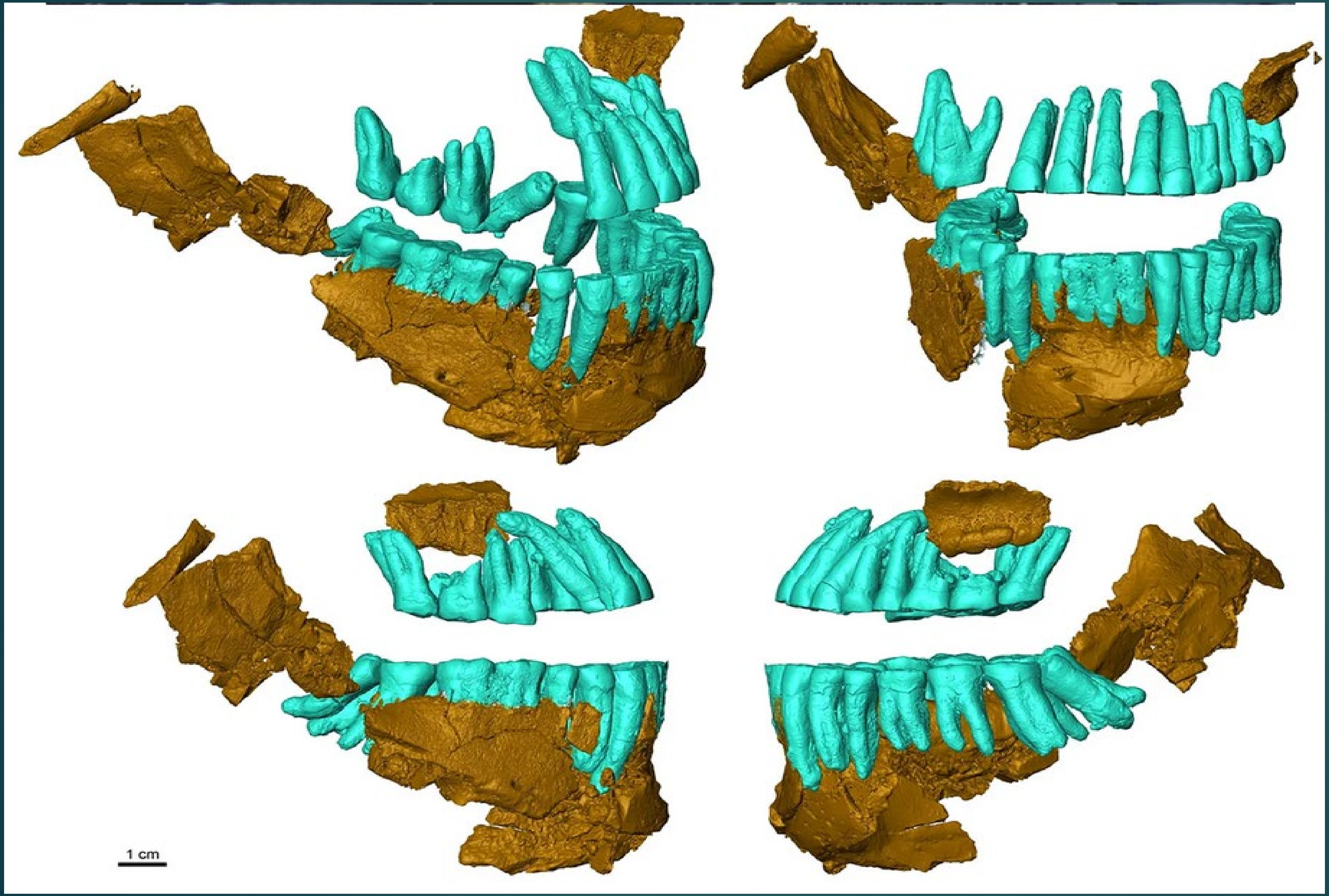
Gibraltar Forbes Quarry female Neandertal, “Nana”



Thorin jaw and teeth: note 2 extra lower molars

The Thorin Neanderthal: the mandible *in situ* when found in September 2019.

Virtual reconstruction of the jaw and dental elements of Thorin



Had two extra lower molars.

This trait is sometimes suggestive of an inbred population?

Thorin = 42 Ka

- Thorin lived between 50,000 and 42,000 years ago.
- Molecular analysis of his remains, including a molar, revealed that about 65% of Thorin's genome could be recovered.
- The population of Thorin had spent 50 millennia without exchanging a single gene with the classical Neanderthal populations.
- "We thus have 50 millennia during which two Neanderthal populations, living about ten days' walk from each other, coexisted while completely ignoring each other."

High homozygosity = lots of inbreeding

- Thorin had high genetic homozygosity — identical gene variants often indicative of recent inbreeding — and no evidence of interbreeding with modern humans.

- Results suggest small group sizes and long-term genetic isolation of the Thorin population from other late Neanderthal populations.

- Evidence newly uncovered in 2023 suggests Thorin is much more likely to be 42,000 years old and therefore is among the very last Neanderthals. 1 of only 5 late N skeletons

A Separate Line of Neanderthals in Southwestern Europe

- This newly identified lineage of Neanderthals, to which Thorin belonged, seems to have lived in small, closely related communities that exchanged mates only within their own group.

- Thorin’s DNA shares similarities with that of a Neanderthal fossil found in Gibraltar, suggesting that this isolated population may have stretched across parts of southwestern Europe.

N diversity

- As Thorin’s lineage demonstrates, Neanderthal populations were not as uniform as once believed.

- Slimak said that the discovery suggested that Neanderthal communities were small and insular — factors that could be key to understanding their extinction because isolation is generally considered to be an evolutionary disadvantage.

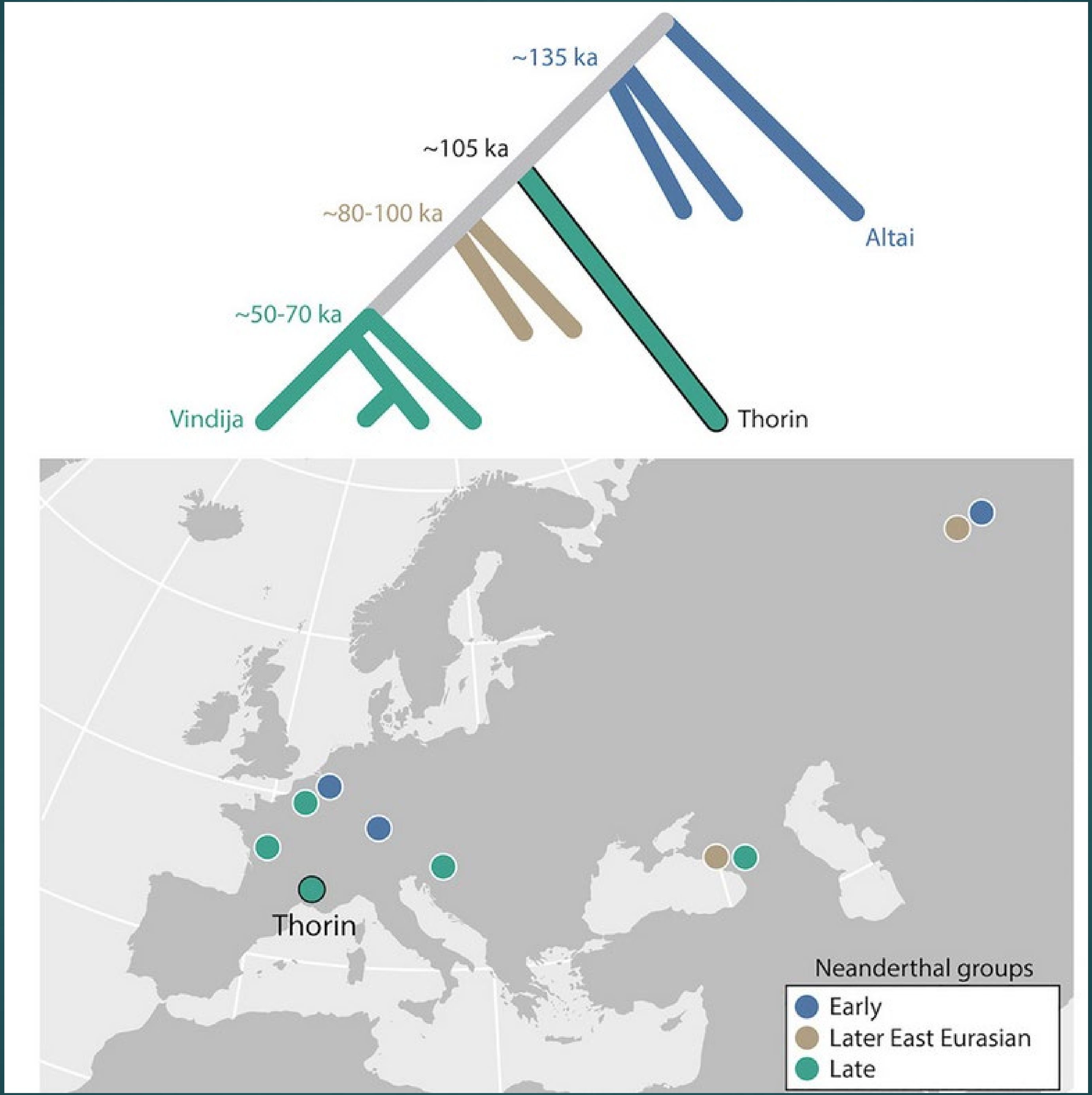
- Sikora, M., Slimak, L., Hopfe, C., Feuerborn, T. R., Havik, B., Makowsky, R., … & Prüfer, K. (2024). *A previously undescribed late Neanderthal lineage from the Grotte Mandrin site*. *Cell Genomics*, 4(10)

Genome

- It should be noted that paleogenomic and osteological studies have revealed low effective population sizes and signatures of inbreeding in Siberian and late European Neanderthals, suggesting social structures characterized by small group sizes and low intergroup mobility.

- This contrasts with recent results from early Eurasian modern humans, which showed low levels of inbreeding and higher intergroup mobility despite small group sizes.

- Whether these results are representative of wider Neanderthal and modern human social organization remains inconclusive.


~135 ka
~105 ka
~80-100 ka
~50-70 ka
Altai
Vindija
Thorin
Thorin
Neanderthal groups
● Early
● Later East Eurasian
● Late

Separate lineages

- The deepest divergence among Neanderthal genomes sequenced to date is found between eastern and western Eurasian Neanderthal populations represented by the ~120 ka Altai Neanderthal from Denisova Cave and the >44 ka Vindija 33.19 individual from Croatia.
- The earliest in western Europe being ~120 ka (Scladina and Hohlenstein-Stadel (HST)), while the latest being ~40 ka, suggest genetic continuity in western Eurasia for ~80 ka.
- Recent results obtained from sedimentary DNA suggest that the genetic landscape was significantly altered by expansions of Neanderthal populations ~105 ka. This gave rise to lineages in western Europe represented by samples from Central Europe (Vindija), the Caucasus (Mezmaiskaya Cave), and Siberia (Chagyrskaya cave 8), the latter likely replacing the earlier Altai-like population

Vindija Ns

- Genomes of late (<50 ka) European Neanderthals, including an individual from the Caucasus (Mezmaiskaya 2), were all found to be more similar to Vindija than to other known lineages, indicating further population turnover towards the last stages of Neanderthal history in the Caucasus or western Europe.

- Suggests an absence of major population structure among the sampled late Neanderthal populations. It remains unknown whether these patterns result from long-term in situ evolution of late European Neanderthal populations, or as a consequence of a recent expansion of Vindijalike lineages into Europe.

Separate N groups

- Thorin belonged to a late Neanderthal population which had stayed genetically isolated for some 50 ka.
- Evidence of gene flow from a deeply divergent lineage distinct
- Our results suggest the presence of multiple isolated late Neanderthal communities in Europe close to their time of extinction, and shed light on their social organization with limited, if any, level of interactions in between different Neanderthal populations in their last millennia.

More lineages

- Thorin belongs to a deeply diverging European Neanderthal lineage, representing a remnant of earlier European Neanderthals.

- Interestingly, the divergence of this lineage began at ~100-105 ka, during the MIS 5 interglacial, a period that saw fast climatic and environmental changes across Eurasia and repopulation by warm adapted fauna through the continent.

Stone tech type indicates separate N lineages

- From MIS 5 to 3 these French Mediterranean Neanderthal societies possessed a distinct technical background.

- Results thus also shed light onto the social organization of Neanderthals, suggesting that small isolated populations with limited, and potentially without, inter-group exchange as a possibly more general feature of Neanderthal social structure.

Slimak’s theory

- Socially speaking, the absence of recent H. sapiens introgression within late Neanderthal populations could have been part of a larger pattern affecting the latter, which seem to have limited or avoided gene exchange not only with early H. sapiens but, more generally, within Neanderthal populations themselves.
- Anthropologically, these gene exchange processes are never limited to a love affair between two individuals, but systematically correspond to the alliances that human populations consciously decide to build. The absence of gene exchanges, or their non-reciprocity (presence of Neanderthal genes in the first H. sapiens in Europe, with no reciprocity in the last Neanderthals (MH to N)), raises questions about the social structures that governed these Neanderthal populations.

CJV: Last Neandertals

- Neanderthal 1 – 40 Ka
- Gibraltar 1 – 40 Ka
- La Chapelle-aux-Saints – 50 Ka
- La Ferrassie 1 – 70-50 Ka
- Amud 1 – 61-53 Ka
- Shanidar – 65-45 Ka
- Thorin – 50-42 Ka
- None of the late Neandertals sequenced to date show any evidence for a recent gene-flow from modern humans,

Neandertal genomes to date. Published genome-wide data of 32 Neandertals across their geographical range and dating to between ~430,000 and ~40,000 years ago.

CJV: Number of Neanderthal genomes: small groups, homozygosity

- Vindija 33.19– Croatia – 45 Ka; 1st - composite from 3 Ns; then high coverage genome
- Altai (Denisova 5) – Denisova Cave; 120 Ka – high coverage
- Chagyrskaya 8 – 59-50 Ka – high
- Goyet, Belgium – 43 Ka - high
- Spy – high – 39-37 Ka - high
- Les Cottés - 43 Ka – high
- ______________________________________
- Forbes Quarry, Gibraltar - low quality
- Hohlenstein-Stadel – 250 Ka - low quality
- Okladnikov – low quality
- Mezmaiskaya - 60-70 Ka - low quality
- El Sidròn – chr 21 & some exome sequences

Number of Neanderthal genomes: small groups, homozygosity

- Sima de los Huesos – 430 Ka - low
- Feldhofer – Neanderthal 1 - low
- Scaldina – 120 Ka - low
- Thorin – 50-42 Ka - low
- Denisovan Genome: Denisova 3
- Morphologically unidentified bone: Denisova 11 (Denny), direct offspring of a Neandertal mother and a Denisovan father

Number of Neanderthal genomes: small groups, homozygosity

- Our ability to retrieve DNA from a larger number of Neanderthal individuals has been limited by poor preservation of endogenous DNA and contamination of Neanderthal skeletal remains by large amounts of microbial and present-day human DNA.

- The lack of high-quality Neandertal genome sequences, especially from the center of their geographical range and from the time close to when they were estimated to have mixed with modern humans, limits our ability to reconstruct their history and the extent of their genetic contribution to present-day humans.

Multiple reasons for possible 1-sided genetic exchange

- There are many possible explanations for this one-sided genetic exchange:
  - It could simply be due to sparsity of data, as relatively few Neanderthal genomes have been sequenced; limited sample size
  - Neanderthal DNA may have been more important for the survival of modern humans than the other way round – for example, bolstering immune system function – so was preserved in later generations by natural selection.
  - Difficulty of distinguishing between ancient DNA contamination from modern humans,
  - Possibility that interbreeding between Neanderthals and modern humans happened much earlier in their evolutionary history, not close to the time of Neanderthal extinction;

*** N population splits

- Some late Neanderthals separated from a common ancestor with the Altai Neanderthal around 150 ka and from a common ancestor with Vindija 33.19 about 70 ka.
- The estimates of the population split times from the common ancestors shared with the Denisovan and with modern humans are around 400 ka and about 530 ka, respectively.
- All late Neanderthals and the older Mezmaiskaya 1 Neanderthal share significantly more derived alleles with the Neanderthals who left DNA in MHs than the Altai Neanderthal does

Mateja Hajdinjak, et al., 2018

1-sided exchange reasons

- Genetic drift: Even if some gene flow occurred, it could have been lost over time due to genetic drift, where certain genetic variants become less frequent in a population by chance
- Social practices that resulted in babies born through interbreeding being kept in modern human groups but not Neanderthal ones. Slimak suspects that Neanderthal women were joining the modern human groups, but the reverse didn't happen.
- N's already small populations were losing reproductive age individuals to the other species, without any replenishment in return – a recipe for demographic disaster

*** MH DNA in Late Ns: L. Li, 2024

- *** Developed methods to estimate the amount of human-introgressed sequences in Neanderthals and apply it to whole-genome sequence data from 2000 modern humans and three Neanderthals.
  - estimate that Neanderthals have 2.5 (Vindija N, 44 Ka) to 3.7%(Altai, 50 Ka) MH ancestry, absorbed DNA from modern humans at least twice
  - leverage human-introgressed sequences in Neanderthals to revise estimates of Neanderthal ancestry in modern humans,

L. Li

- Show that Neanderthal population sizes were significantly smaller (20%) than previously estimated – N population was less than 3000.
- Identify two distinct waves of modern human gene flow into Neanderthals: 200-250 Ka, 100-120 Ka, (besides the classic 50-60 Ka)
- Descendants of those early waves of mating between Neanderthals and moderns must have remained with the Neanderthals, so they left no DNA record in the living humans
- Effective population of Neanderthals lowered to about 2400 breeding individuals
- Last Ns were effectively absorbed into MHs

MH DNA in Late Ns: Tishkoff

- Tishkoff study: N DNA contains 6% MH DNA (mostly in noncoding areas)

- ~6% of the Altai Neanderthal genome was inherited from anatomically MH

- *** L. Li, et al., 2024 concludes Neanderthals inherited as much as 7% of their genome from modern humans, including several genes involved in brain development.

- They dated when the two groups mingled: more than 200,000 years ago. These introgressions were repeated 105,000 to 120,000 years ago, and 45,000 to 60,000 years ago.

Châtelperronian was not N

- The techno-cultural traditions of the Thorin population overlap with the Châtelperronian chronology dating to 45–40 ka absent from the Rhône Valley but recognized in a large region stretching from Burgundy to the Mediterranean and Atlantic Spain and that was classically attributed to late Neanderthal traditions.
- In 2023, it was proposed that the Châtelperronian was not of Neanderthal origin but was closely linked with northern Early Ahmarian industries from Lebanon, an eastern Mediterranean tradition closely associated with moder humans.
- The Châtelperronian would then signal a second wave of H. sapiens migration in the continent and should not be associated with Neanderthal populations.

Small populations

- This three-wave model has since been supported by the discovery of a H. sapiens ilium bone in a Châtelperronian layer from Burgundy, north of Grotte Mandrin.

- These data draw a striking picture of late Neanderthals and their coeval H. sapiens populations, where small populations of Neanderthals appear to have been isolated during tens of millennia, both culturally and genetically, leading to an increase in homozygosity levels.

*** John Hawks review of Thorin paper: N diversity

- I've seen people discussing the idea that Neanderthals lived for thousands of generations next-door to each other without ever mixing. That's just wrong.
- Instead, what I find exciting about the Mandrin work, together with findings from other sites, is the diversity among the later European Neanderthals.
- The Mandrin B2 “Thorin” genome clarifies a component of genetic history that wasn't noticed before. had some information about diversity of much earlier Neanderthals, while DNA from later Neanderthals seemed to represent only one branch of population ancestry
- For more than a decade we've. The Thorin data show that later Neanderthals were also genetically diverse.

Genetic diversity in N lineages

- Thorin may have been a distant relative of the skull from Forbes' Quarry, Gibraltar.
- Their comparative work also suggests that an unsampled Neanderthal "ghost lineage" contributed some of the ancestry of the Les Cottes Z4-1514 individual from Les Cottes, France.
-
- What ancient genomes actually show is that the variation of past humans like the Neanderthals was *structured* differently than recent humans.

Within-group and within-genome variation

- We already knew there was diversity among earlier Neanderthals, because of the great degree of genetic differences between later Neanderthals like Vindija 33.19 and the earlier “Altai Neanderthal” of Denisova..
- Recently there has been quite a bit of evidence about the genetic changes among early Neanderthals, including the widespread introgression of African DNA into their populations.
- But while the Altai Neanderthal genome was different from other Neanderthals, its within-genome variation is low. This female individual had more than 300 megabases—a tenth of its genome—in long runs of homozygosity of 8 megabases or more: highly inbred.

Homozygosity = lots of identical genetic basepairs

- Small local group size sometimes contributes to this kind of inbreeding, and cultural preferences about marriage and childrearing also may contribute.

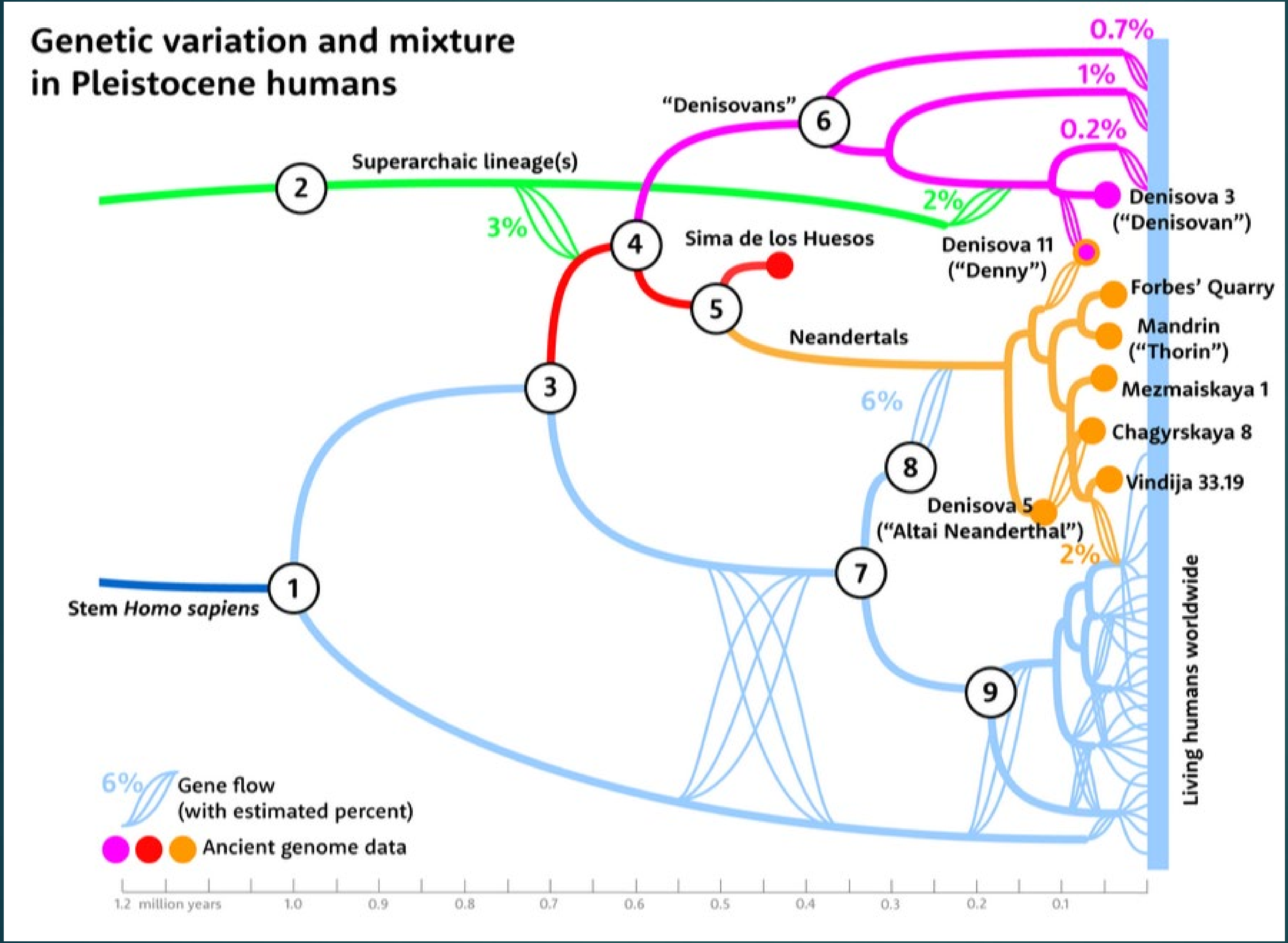
- The Thorin genome with around 100 megabases in long runs of homozygosity is not so extreme. Its genome-wide pattern is similar to people from traditional groups where cousin marriage is frequently practiced.
- One fascinating detail of the Thorin individual is an extra pair of mandibular molars. This is an extremely rare trait in today's humans, But not necessarily result of inbreeding.

Between-population variation

- Between-population genetic variation is a second aspect of Neanderthal population structure.
- A simple measure is counting differences between genomes from different populations, but those differences actually reflect three historical components:
    - the time since the populations first diverged,
    - the amount of gene flow after they diverged, and
    - the genetic variation shared by both populations from their common ancestors.
- The last of these is just within-population variation from both populations' shared past.
- So to consider the between-population components, geneticists do more than just count, they fit data to a population model.

Model for estimation divergence

- Slimak and coworkers applied a model to estimate when the populations ancestral to the Thorin genome and the high-coverage Vindija 33.19 genome might have diverged.
- That estimate is just before 100,000 years ago,
- The Thorin individual lived sometime between around 52,000 and 48,000 years ago. The Neanderthals from Vindija, Croatia, were slightly later in time, meaning that the shared common ancestors of Vindija 33.19 and Thorin lived around 50,000 years earlier than either of these individuals.



The Thorin genome (grouped together with the Forbes' Quarry skull) adds to the diversity of later Neanderthals.

The diversity among these groups was still less than within modern African populations or among Denisovan populations.

Dynamic populations

- A third aspect of population structure: static versus dynamic structure.
- Grotte Mandrin and Vindija are around 1000 km from each other. Genomes from these two places seem like they should be closer to each other than either is to Chagyrskaya Cave, nearly 6000 km from Vindija. But that's not the case. Instead, the Vindija 33.19 and Chagyrskaya 8 genomes share more recent ancestry and Thorin is the odd genome out.
- If the population structure was *static*, not changing over time, then this pattern of similarities and differences would suggest some kind of barrier reduced gene flow between Neanderthals in Croatia and southern France.
- But in my view the situation is more easily explained by a *dynamic* population structure, in which some populations expanded in geographic range while others contracted over time.

Dynamic Ns at Altai

- The dynamic explanation has long been at play for the central Asian Neanderthals.

- For example, while Thorin and Vindija 33.19 are fairly different from each other, the genome of the "Altai Neanderthal"(Denisovan 5), diverges from both.

- Denisova Cave is less than 200 km from Chagyrskaya Cave. But the Denisova 5 individual lived thousands of years earlier than Chagyrskaya 8. The great difference between Denisova 5 and Chagyrskaya 8 is easily explained if the common ancestors of Vindija and Chagyrskaya Neanderthals expanded their geographic range into areas that earlier were occupied by more distantly related groups.

Different N populations

- In the dynamic scenario, the Altai saw a succession of different Neanderthal populations.
- It wasn't only Neanderthals. Other evidence from Denisova Cave shows that multiple Denisovan populations left biological evidence within this one site over hundreds of thousands of years.
- The Denisova 11 hybrid individual, with a Neanderthal mother and Denisovan father, shows that these groups sometimes were in the area at the same time.

Bottom line

- “Long genetic and social isolation in Neanderthals before their extinction” is the title of Slimak and coauthors' article. This title calls back to an old idea.
- According to this idea, Neanderthals evolved anatomical specialization in Europe while isolated from humans in other regions. Many anthropologists have written about this idea. Some scientists over the years challenged it.
- The Thorin genome suggests that the Neanderthals of 50,000 years ago were not a dwindling relict. The deep histories of their populations were like small-scale human populations that still live in Africa.

Ns had high homozygosity

- The Thorin genome *increases* our estimate of genetic variation across the Neanderthal geographic and temporal range.

- Later Neanderthals were more like earlier Neanderthals in diversity than we knew. Meanwhile, Neanderthal mating patterns seem to have been like small-scale human groups that practice cousin marriage.

- Individual Neanderthal genomes had higher homozygosity than the average human living today, a result of high genetic drift in local populations. This would weaken purifying selection against deleterious genetic variants.

Genetic load

- The buildup of deleterious variants may impede survival and reproduction, a phenomenon known as *genetic load*. Some researchers have suggested that such deleterious variants could not persist in human populations, limiting our Neanderthal genetic heritage.

- I would say that the Thorin genome gives a valuable clue about how Neanderthals made this demographic situation work. Divergent populations are repositories for genetic variation. Mixture between divergent populations provided opportunities for the *rescue* of small populations from genetic load. New variants might sometimes *correct* the biological problems caused by the buildup of deleterious variants. Again, occasional interbreeding would spread such adaptive variants.

European Ns had 2 branches

- Deep lineage diversity characterized regional populations of humans throughout our Pleistocene history. Within Africa, among Denisovans, and among Neanderthals, we can see deep branches. Thorin's genome shows that late European Neanderthals had at least two deep branches. That's one more than we knew about two years ago.
- Aaron Ragsdale points out that most approaches do not actually distinguish long-term isolation of lineages—including supposed “ghost populations”—from isolation-by-distance or other hypotheses with restricted gene flow.
- Declaring 50,000 years of isolation based on a single genome is not generally realistic unless models with long-term gene flow are clearly rejected by the data.

End October CAS

*** An emerging consensus in paleoanthropology: demography was the main factor responsible for the disappearance of Neanderthals

- The causes of Neanderthal disappearance about 40,000 years ago remain highly contested. Over a dozen serious hypotheses are currently endorsed to explain this enigmatic event. Given the relatively large number of contending explanations and the relatively large number of participants in the debate, it is unclear how strongly each contender is supported by the research community.
- What does the scientific community actually believe about the demise of Neanderthals? To address this question, we conducted a survey among practicing paleo-anthropologists (total number of respondents = 216). It appears that received wisdom is that demography was the principal cause of the demise of Neanderthals. In contrast, there is no received wisdom about the role that environmental factors and competition with modern humans played in the extinction process; the research community is deeply divided about these issues.

•Krist Vaesen,, Gerrit L. Dusseldorp & Mark J. Brandt, 2021

Reason for demise of Ns

- Numerous hypotheses have been advanced to explain the disappearance of Neanderthals.
- According to a first category of hypotheses, the event was causally related to the migration of modern humans into territories occupied by Neanderthals: resident bands of Neanderthals and incoming bands of modern humans found themselves in competition for the same limited resources. A competitive advantage for modern humans then resulted in the replacement of Neanderthals by the principle of competitive exclusion.
- This category of hypotheses comprises several variants, distinguishable by the type of competitive advantage they postulate. The inter-specific difference might have been morphological, cognitive, technological, social or economic.

Demographics

- A second category pertains to hypotheses that refer to the internal, demographic dynamics of Neanderthal populations. Even in the absence of competition with modern humans, Neanderthal populations might, generally, have been too small to persist in the long run.

- More specifically, their small size and limited interconnectedness would have made them highly susceptible to inbreeding (viz., reduction in fitness of individuals that arise from matings between genetic relatives), Allee effects (reduction in population growth rates due to problems in mate-finding), and stochastic fluctuations (sudden drops in population size due to random fluctuations in births, deaths and sex ratio).

Survey of researcher opinions

- A final, third, category attributes the demise of Neanderthals to environmental factors. These factors include general climatic instability, extreme climatic conditions due to volcanic activity, the introduction of pathogens by modern humans into the immunologically naive Neanderthal population.

- Conducted a survey among practicing paleoanthropologists. We presented respondents (total number = 216) a list of factors that might have contributed to the disappearance of Neanderthals, and asked them to provide their estimate of the strength of each factor's contribution.

Political prejudices?

- Second aim of our study was to assess correlations between respondents’ views about Neanderthal extinction and a set of social psychological constructs that capture people’s socio-political attitudes.

- The following considerations motivated us to run such a test. The picture that emerges from at least some of the relevant literature (see the exchange between Villa, Zilhão, Wynn, etc.) is one of a highly polarized debate, that is divided in ‘tribal’ camps, each defending its own theory.
- Response rate = 29%

Zilhão vs Wynn

- By way of illustration consider the positions of Zilhão and Wynn et al.. The two parties disagree about the cognitive differences between modern humans and Neanderthals: whereas Wynn and colleagues claim that differences in the cognitive abilities of modern humans and Neanderthals were visible to natural selection,
- Zilhão believes that the two species were indistinguishable. It could be the case that, as Zilhão believes, such a difference of opinion has its roots in a difference of opinion about human progress; it could be that, as Zilhão writes, there exists “a persistent, if subconscious influence in academia of Victorian-age ideas of evolution-as-progress and ancientas-primitive”. On Zilhão’s account, claims that Neanderthals are not quite like us betray an outdated form of hierarchical thinking.
- On Wynn et al.’s account, claims that Neandertals were indistinguishable are rooted in extreme anti-science versions of contemporary social justice theory.

Demise Causation = Demographics>Environment>Competitive

- Causal contribution of demographic factors to the demise of Neanderthals is stronger than the contribution of environmental factors, and that the contribution of the latter is stronger than the contribution of competitive factors
- Population size has the most support
- Competitive factors “Economic advantage”, “Technological advantage” and “Cognitive advantage” are among the lowest ideas.
- Social views do not appear to be meaningfully correlated with researchers’ positions on this debate.

Conclusions

- Demographic factors are generally considered to be the most salient in accounting for the disappearance of Neanderthals. Our expert sample thought the strength of the causal contribution of demography to be larger than the strength of the contribution of either environmental of competitive factors: the DEM >ENV and COMP composites.
- The individual factor with the highest score appeared to be a demographic one, Environmental factors are the runner-up: ENV scored significantly higher than COMP, and climatic factors ranked second in the ranking of individual factors (i.e., before any competitive factor).
- Few believe it was competition.

Received wisdom is recent

- So, what is the received wisdom among practicing paleo-anthropologists? The high consensus scores for demography suggest that the current received wisdom pertains to demography; the disappearance of Neanderthals was primarily driven by demographic factors.
- This is surprising, given that, according to a recent review of the literature, virtually all archaeological studies of the Neanderthal-H. sapiens transition that have explicitly evoked a causative role for such factors were published in the last decade most of these studies even came out just during the past 5 years. In fact, demography has only very recently been shown to be sufficient to account for the demise of Neanderthals

No received wisdom regarding other possible causal factors.

- There is no received wisdom regarding other possible causal factors. The disagreement over the supposed cognitive, technological, social, economic advantages of modern humans over Neanderthals that characterizes the aforementioned exchange between Villa and Roebroeks, Zilhão, and Wynn et al., does not seem to be just a disagreement among a couple of individuals, rather, these issues appear to divide the entire research community.
- This finding is at odds with Breyl's literature review. According to Breyl, the received wisdom among paleo-anthropologists is that Neanderthals were cognitively and technologically comparable to modern humans.
- Did not find any correlation between respondents' socio-political views and their views about competitive causal factors (or any other causal factor, for that matter).

Politics do not determine scientific ideas; lack of data does

- Finding that socio-political presuppositions, or at least presuppositions along the traditional left–right political spectrum, do not determine archaeologists' scientific views is interesting also in the sense of refuting the complaint that anthropology is nothing but politics disguised as science.
- As far as our results go, disagreements about the demise of Neanderthals are scientific disagreements; arguably, they primarily result from the general difficulties in inferring behavioral and other traits from a low-resolution and poorly preserved archaeological record.

*** Ancient humans were so good at surviving the last ice age, they didn't have to migrate like other species

- Humans seem to have been adapted to the last ice age in similar ways to wolves and bears, according to our recent study, challenging longstanding theories about how and where our ancestors lived during this glacial period.
- Previous studies have supported the view of most archaeologists that modern humans retreated into southern Europe during the height of the last ice age and expanded during the later increase in global temperatures.
- But this study is the first to use genetic data to show that at least some humans stayed in central Europe, unlike many other animals and despite our species having evolved in the much warmer climate of Africa.

Climate and animal distribution

- Scientists have known that the distribution of animals and plants across the world may fluctuate with the climate.
- Many species, including humans, expanded their geographical ranges since the height of the last ice age, approximately 20,000 years ago.
- Reviewed the genetic history of 23 common mammals in Europe. In addition to humans, these included rodents such as bank voles and red squirrels, insectivores like shrews and hedgehogs, ungulates like red deer and wild boar, and carnivores like brown bears and weasels.
- Areas of high genetic variation are likely to be the areas of longest occupation by species. These areas, known as refugia, are locations where species retreated to survive during periods when environmental conditions were unfavorable elsewhere. These refugia were probably the warmest areas or places where it was easiest for the animals to find food.

Widely distributed

- Four general patterns emerged among European mammals: an east–west decline in variation, a Western-Central belt of the highest diversity, southern richness, and homogeneity with no geographic pattern.
- Study indicated some species (such as brown bears and wolves) were already widely distributed across Europe during the height of the last glaciation with either no discernible refugia or with refugia both to the north and south.
- This pattern includes Homo sapiens too. Neanderthals had already been extinct for around 20,000 years by this point.
- But they seemed able to tolerate the ice age conditions while other animals withdrew to refugia.

Modern Humans

- It is unclear whether these humans relied on ecological adaptation, for example, the fact that they were omnivorous meant they could eat many different things, or whether they survived due to technology.
- For instance, it is well established that humans had clothing, built dwellings and controlled fire during the cold conditions of the last ice age.
- It could mean that some areas may be habitable for longer than expected as the climate changes.

*** Reconstructing contact and a potential interbreeding geographical zone between Neanderthals and anatomically modern humans

- The timing and geography of interbreeding of Ns and MHs are not clearly known. In this study, we applied ecological niche modelling and GIS (mapping software) to reconstruct the paleodistribution of Neanderthals and AMHs in Southwest Asia and Southeast Europe and identify their contact and potential interbreeding zone during marine isotope stage 5 (MIS 5) (120 to 80 kyr), when the second wave of interbreeding occurred.
- Used climatic variables characterizing the environmental conditions of MIS 5 along with the topography and coordinates of Neanderthal and modern human archaeological sites to characterize the paleodistribution of each species. Overlapping the models revealed that the Zagros Mountains were a contact and potential interbreeding zone for the two human species.

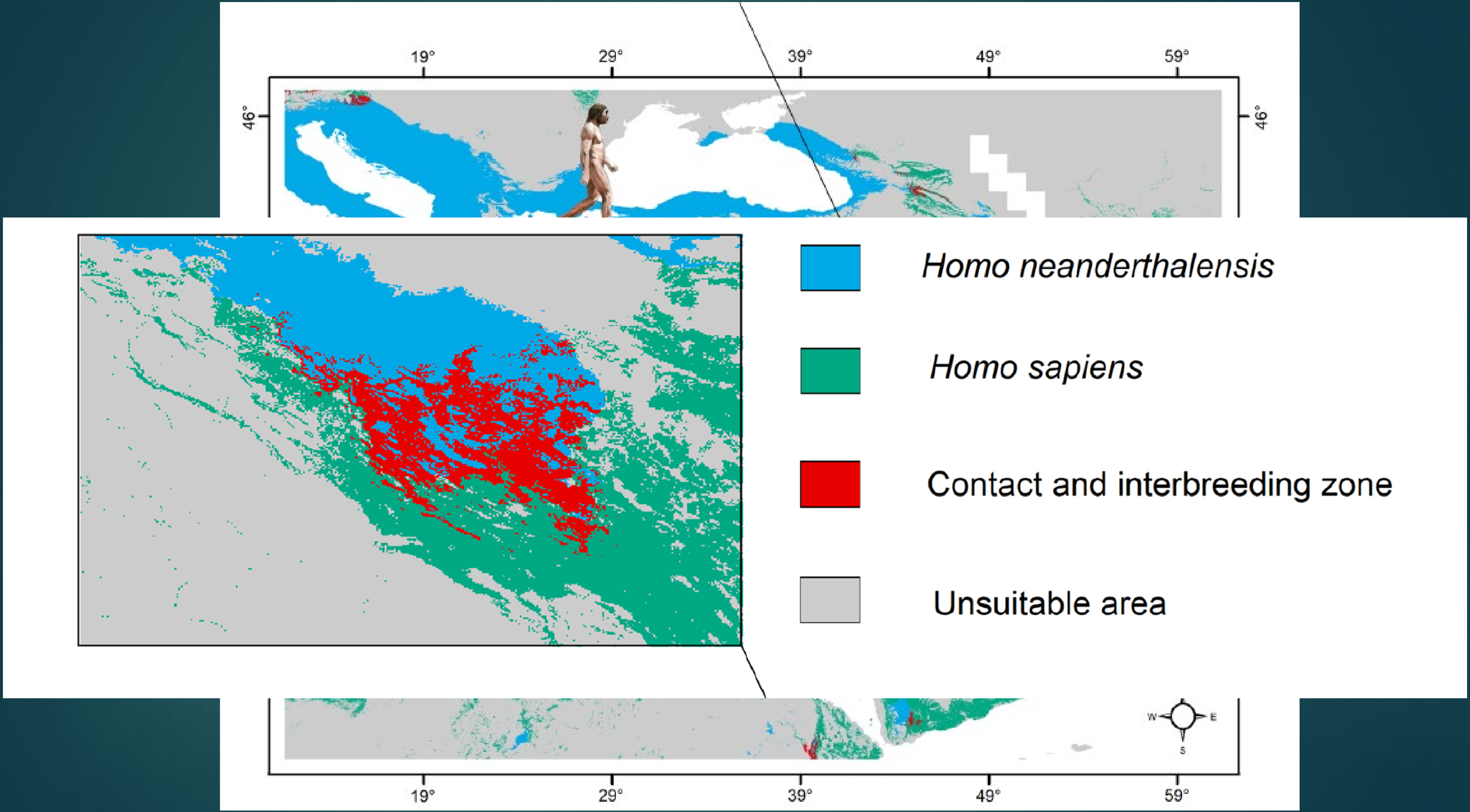
Saman H. Guran, et al., 2024

Zagros Mountains

- The Zagros Mountains stretch across present-day Iran, northern Iraq (Shanidar Cave), and southeastern Turkey. The region's diverse biodiversity and varied topography would have supported large, stable human populations, making it an ideal meeting place. It acted as a natural corridor, connecting the cooler Palearctic realm with the warmer Afrotropical realm, thus facilitating human migration and interaction.
- We believe that the Zagros Mountains acted as a corridor connecting the Palearctic/Afrotropical realms, facilitating northwards dispersal of AMHs and southwards dispersal of Neanderthals during MIS 5.
- There is strong evidence of multiple interbreeding events between two groups of Neanderthals and archaic/ modern humans in western Eurasia. Paleogenetic studies have shown that the second wave of interbreeding occurred during MIS 5 .

Contact area

- In some studies, researchers have suggested that the lower latitude regions of southwestern Asia have high potential for the first overlap between Neanderthals and AMHs. They shared the same ecological niches under certain climatic conditions during the Late Pleistocene. Recently, Churchill et al. reported facial morphological similarities between Neanderthals and AMHs in the Near East, indicating it could be a key region for interbreeding between the two lineages. However, it is still unclear where the two species met and interbred.
- The aim of the present study was to reconstruct the paleodistribution of Neanderthals and AMHs during MIS 5 to identify the contact and potential interbreeding geographical zones of these two species



🟦 *Homo neanderthalensis*

🟩 *Homo sapiens*

🟥 Contact and interbreeding zone

⬜ Unsuitable area

A refugia area

- For the first time, we applied ENMs as additional and independent lines of information to locate possible geographic locations where the two species interbred.
- Our study identified the Persian Plateau, particularly the Zagros Mountains, as a potential interbreeding area for AMHs and Neanderthals. The possibility of attracting different hominin groups in the Zagros Mountains is justified by the geographical conditions of this region, since it is located in two different biogeographical zones, namely, the Palearctic and Afrotropical realms. The border areas of two realms are important in biology since they operate as refugia for species from glacial environments.
- Consequently, some parts of the Zagros Mountains could have been visited repeatedly by people living in the border areas of the Palearctic and Afrotropical realms during Pleistocene climatic shifts. Therefore, the possibility of interaction between different hominins, including AMHs and Neanderthals, was greater in these areas.

*** The evolving three-dimensional landscape of human adaptation: Hominins preferred rough terrain

- Over the past 3 million years, humans have expanded their ecological niche and adapted to more diverse environments. We show that human sites clustered in areas with increased terrain roughness, corresponding to higher levels of biodiversity.

- We find a gradual increase in human habitat preferences toward rough terrains until about 1.1 Ma, followed by a 300 thousand-year-long contraction of the ecological niche.

- This period coincided with the Mid-Pleistocene Transition and previously hypothesized ancestral population bottlenecks.

Expansion

- From 0.8 Ma onward, the human niche expanded again, with human species (e.g., *H. heidelbergensis*, *H. neanderthalensis*, and *H. sapiens*) adapting to rougher terrain, colder and drier conditions, and toward regions of higher ecological diversity.
- According to our analysis, area roughness is the most important predictor of human biome diversity at sites of hominin occupation, exceeding even the contributions of the key climatic variables temperature and precipitation
- This result supports the notion that terrain roughness (slope) is an important predictor in hominin studies and niche modeling.

Terrain slope

- Human adaptation toward increasing area roughness occurred in two major phases:
  - The first one, from 2 to 1.1 Ma, was interrupted by a substantial decrease during the MPT.
  - The second adaptation phase, 0.9 to 0.1 Ma, coincided with the expansion of H. heidelbergensis and H. neanderthalensis into Europe and the general positive trend in the brain size of hominins

Niche contraction

- The niche contraction during the MPT, which occurred mostly in Africa, coincided with several major evolutionary events.
- In Africa, recent studies suggest a human population bottleneck, which reportedly reduced the genomic diversity of humans by a factor of ~80.
- The timing also roughly matches with estimates of when the fusion of human chromosome 2 (found in Denisovans, Neanderthals, and Homo sapiens.).

Hominins preferred rough terrain

- The areas with medium and high roughness are particularly abundant with diverse food resources, environmental niches , and potential natural shelters to mitigate weather and climate extremes. These characteristics may have contributed to the survival and overall evolution of the genus Homo, increasing their resilience and versatility.
- Living in sloped regions could also translate into reduced energy expenditure required for foraging, as prey can be detected more easily from afar and the increased food diversity means that individuals can obtain provisions more efficiently within their immediate vicinity.
- In this scenario, individuals could have allocated more time and resources to other activities, such as social interactions or tool production.