'Neanderthal Man' — Nobel Prize winner Svante Pääbo revolutionized anthropology. Here is a look back at his groundbreaking 2014 memoir



vante Pääbo's memoir of how he came to lead a project to sequence the Neanderthal genome— <u>Neanderthal Man: In Search of Lost Genomes</u>— is at heart about sex. Sex in the sense of sexual behavior, not biological sex.

Sex in the sense of the drawn-out process of discovering whether we, the anatomically modern humans who are the sole survivors of the genus *Homo*, ever mated and produced children with our extinct nearest relative.

And-let's deal with this first and get it out of the way-sex in the sense of Pääbo's own sex life. His candor about his bisexuality and his lengthy affair with a (female) scientist who also happened to be the wife of a colleague/collaborator who was nearly as well known in evolutionary genetics as Pääbo himself. An affair that resulted in a son and marriage on a remote beach in Hawaii. Told with a strong implication that it wasn't that big a deal. That they all lived happily ever after.

A novelty in scientific autobiography, to be sure, and bound to raise more than a few eyebrows. But the candor reveals no drama and recounts no prurient details. Not about his gay life and not about the events leading to that private romantic marriage. Instead, they are matter-of-fact disclosures. Very nearly ho-hum.

This struck me as being fully in line with the trend in public attitudes toward sexual preferences, in the West at least. Which is a shrug and "whatever." A revolution, really, but radical chiefly in that it has happened so fast. Fast, but not so fast that it has spilled over into places like Russia and Uganda.

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Did we have sex with Neanderthals?

Of course. You don't need to look at genomes to figure that out. "[W]hat human groups don't?" Pääbo asks, rhetorically. So, yes, we had sex with them.

But did we have children with them? That's the really interesting question. If Neanderthal DNA lives on in us, then it can be said that Neanderthals are not really extinct after all. It could mean we got some useful stuff from them; it would be good to know what it was. And scientists could begin to figure out which genes we possess that they didn't, how and why those genes contributed to the fact that we're here, several billion of us, and they are long gone.

There was scientific resistance to this idea of intromission, the decorous term scientists use. Pääbo himself doubted it. That's partly because the first stab at Neanderthal DNA some years ago was to sequence the mitochondrial genome, not the DNA in the cell nucleus. (Nuclear DNA is what we usually

mean when we say "the genome.") Neanderthal mtDNA turned out to be unlike any human mtDNA around today. Which suggested that Neanderthals had contributed nothing to us.



Mitochondria, generally called the energy powerhouses of a cell, are remnants of bacteria that invaded multicellular organisms billions of years ago and stuck around. (For <u>more on mtDNA</u>, <u>see my GLP article</u> <u>on "three-parent" babies</u>.) If mtDNA is not "the genome," why bother with it? Because, although it contains only 37 genes, there are hundreds and sometimes thousands of copies of it in every cell. There's only one copy of "the genome," the DNA in the cell nucleus. It's much, much easier to recover mtDNA, especially if you're trying to pry fragile DNA from bone that's been lying around in a cave for 40,000 years or more.

Even though Neanderthal mtDNA isn't like ours, the only way to really settle the question of its genetic contribution to us is to look at DNA in the Neanderthal cell nucleus and see if any of it matches our DNA. That horrendous task is mostly what *Neanderthal Man* is about.

The result: People of European or Asian ancestry have inherited between 1 and 4 percent of their nuclear DNA from Neanderthals, probably from matings that took place in the Middle East–in present-day Israel, in fact–before the forebears of Europeans and Asians dispersed to the West and East. For technical theoretical reasons, it seems likely that most of these matings involved Neanderthal men with women from what Pääbo calls the Replacement Crowd. (That's us.)

The task: Herculean. Monumental. A slog.

I've written a number of pieces on ancient DNA, and I've always known it was tough to find and to analyze. But from *Neanderthal Man* I learned that I had no idea. DNA can be destroyed easily; ancient

bone sources are pretty useless unless they've been very dry for their thousands of years of storage. It also helps if they are very cold, which is why bones from extinct mammoths have yielded DNA relatively easily. There are no Neanderthals buried in permafrost.

And then there's the contamination problem. Microbes, mostly bacteria, burrow into buried bone and leave their DNA behind. So do the workers who dig up the bones and the museum curators who handle them (and sometimes <u>lick them</u>, a practice that, when he witnessed it himself, nearly caused Pääbo to faint dead away.) Recent human DNA contamination is particularly awful because it's so similar to Neanderthal DNA; it's terribly hard to tell them apart.

And when the scientists finally got probable Neanderthal DNA, the tiny fragments had to be run through sequencers hundreds (or thousands) of times to ensure accuracy. The resulting sequences then had to be mapped against contemporary human DNA and ape DNA to figure out where they differ. This, Pääbo says, is "much like doing a giant jigsaw puzzle with many missing pieces, many damaged pieces, and lots and lots of extra pieces that would fit nowhere in the puzzle."

I'm not even going to get in to the computations and programming skills involved in every step, although Pääbo explains them quite well even for the mathematically uninclined.

In fact, the explanations of technical matters throughout the book are on the whole admirable. A few scientists write really well, but most don't, and English is not Pääbo's first language. You wouldn't know it. Some passages made me wonder if a science writer had helped out. Four editors are credited in the brief Preface, but no science writers. Pääbo is free with praise and thanks for his many scientific collaborators, so I'm inclined to think he would do the same for significant writing help if he had gotten it. I guess that's a compliment, but maybe I'm just envious.

The team: Cohesion, cooperation, and gratitude

Pääbo emphasizes how important his lab team's cohesion was to him. He is quite snarky about the two 800-pound gorilla journals, *Science* and *Nature*, which have been so eager to be known for hot papers that they have published some dubious ancient DNA studies. (One example is a most unlikely claim to have sequenced dinosaur DNA.) Yet a number of important papers from his lab have appeared there, in part because those venues do the careers of his junior colleagues the most good.

Another example: He and some of his colleagues wanted to patent the Neanderthal genome and license its use elsewhere, especially for use by companies providing DNA sequencing as a consumer product. This money would help fund the lab's work. But some in his research group were adamantly opposed, insisting the data should be available freely to all. Pääbo bowed to their urgency and gave up the patenting idea.

Cooperation was a hallmark among the many far-flung collaborators too. In the time leading up to publication of the complete Neanderthal genome paper, Pääbo feared that the startling news about Neanderthal DNA being found in most of today's humans would leak to reporters. But it never did. Quite remarkable, considering that at least 50 people knew this fascinating fact. That paper, by the way, was

nearly book-size. The supplementary material ran to 19 chapters and 174 pages.

It's an interesting question how much the research in Pääbo's lab (at the Max Planck Institute for Evolutionary Anthropology in Leipzig) was eased along by something most of today's scientists are not vouchsafed: stable support. It came from Germany's Max Planck Society. This is funding that doesn't require the anxiety and hassle of annual grant proposals.

Svante Pääbo and the Platonic Idea of research

I don't know if this is the real Svante Pääbo: driven, obsessive, a team-building natural, honest about his errors and his anxieties and his (very occasional) fits of temper. Often modest. The very model of a modern major scientist, and a very nice guy.

I hope so and have no reason to think otherwise. Personal anecdote: Several years ago an editor introduced a fairly serious error into a piece I had interviewed him for. She then posted the final version before I had a chance to look at it. When I did, I was of course horror-struck. I demanded (and got) an immediate fix, and then, visions of my science journalism career in ruins, wrote Pääbo a groveling apology. He replied by return email, amused at my panic, telling me not to worry. Whew!

So, yes, to this *n* of 1, a very nice guy.

Pääbo's tale describes a process approaching the Platonic Idea of contemporary science: a lot of very smart people collaboratively working their butts off, persisting through mistakes and failures and numbingly repetitive but essential tasks and political machinations and technological inadequacies because they believe the Truth is Out There. And finally finding it.

Others have not yet weighed in, and this being top-level and therefore monumentally competitive science, contrarians may well emerge. But if the Neanderthal genome project was anything like what Pääbo describes, we are damn lucky.

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