Why almost everybody has a MTHFR mutation.

A lot of guff is written about how mutations in the gene for the MTHFR enzyme (also called MTHFR) can have terrible effects. One would think that anybody with a MTHFR mutation must be lucky to be alive. But you almost certainly have at least one mutation in that gene.

The genetic analysis program Promethease lists 16 SNPs (Single Nucleotide Polymorphisms – the posh name for places that mutations can happen) for the MTHFR gene. Of those, it lists the frequencies with which those mutations occur for 15 SNPs. We can use that to calculate the probability of not having any of those mutations. I've used the probabilities for those with Northern and Western European Ancestry.

The probability of not having a mutation at location rs1801133 is 46.9% (or 0.469).

The probability of not having a mutation at location rs4846049 is 38.5% (0.385)

Of the 46.9% with no mutation at rs1801133, only 38.5% of them will also have no mutation at rs4846049. That means that 0.469 x 0.385 = 0.180 (18%) will not have a mutation at either location. Already we have 82% having at least one mutation at one of those two locations.

If we continue the sum for the other 13 locations we get.

0.469 x 0.385 x 0.619 x 0.487 x 0.460 x 0.496 x 0.690 x 0.903 x 0.690 x 0.761 x 0.905 x 0.892 x 0.885 x 1.00 x 0.434 = 0.00126 (0.126%)

That means that 99.874% of people **do** have at least one mutation on those 15 locations. That is just 8 people in a thousand who do not have a mutation.

How has the human race survived with all those people carrying such terrible mutations? Obviously those mutations are not so terrible. Indeed, most mutations do little or no harm. There is just one mutation that might possibly be harmful, according to the testing company 23andMe, and that is homozygous for the C677T mutation, carried by 9% of the population.

Here's an example of how the calculation is done.

Suppose that 20% of all people have a mutation at any one of 10 locations on a gene.

So, 80% of people do not have a mutation at location 1.

And 80% of those do not have a mutation at location 2 either. That's 80% of 80% = 64%

Of those, 80% do not have a mutation at location 3. That's 80% of 64% = 51.2%

Already, almost half of people have at least one mutation at locations 1, 2 or 3.

Location 4 = 80% of 51.2% = 41%

Location 5 = 80% of 41% = 32.8%

Location 6 = 80% of 32.8% = 26.2%

Location 7 = 80% of 26.2% = 21%

Location 8 = 80% of 21% = 16.8%

Location 9 = 80% of 16.8% = 13.4%

Location 10 = 80% of 16.8% = 10.7%

So, even with a fairly low incidence of mutation, at just 10 locations, almost 90% of people have at least one mutation.