Human Family Tree
Mitochondrial Eve

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Abstract—**Cann, Stoneking and Wilson as described in their paper [2] on Mitochondrial DNA and human evolution used 147 human mitochondrial DNA (mtDNA) samples, and performed restriction mapping on each sample. The restriction sites were mapped using known human mtDNA sequences. The number of restriction site differences between each pair of individuals gave them the extent of the nucleotide sequence divergence. mtDNA is inherited from the mother and unlike nuclear DNA, does not go through combination of DNA from both the parents. All living human beings are thought to have descended from one common ancestor [3]. This is not to be thought of as a specific person, since whenever an ancient mtDNA branch dies out, the most recent common ancestor (MRCA) moves to a more recent female ancestor. The restriction site differences between all the pairs of individuals were used to induce a genealogical tree shown in figure 1. This tree suggested that human beings originated in Africa and then settled the rest of the planet as shown in figure 3. The aim of the project is to start with mtDNA samples from a varied group of people and compute the alignment distance matrix for all pairs of samples. Using this matrix, an evolutionary tree and hierarchical clustering algorithm needs to be implemented in order to induce a tree similar to the one shown in 1.**

I. BIOLOGICAL PROBLEM AND ITS SIGNIFICANCE

mtDNA is comprised of 16,569 base pairs and is present only in cells in the animal kingdom. It is contained in almost every cell of the body and is inherited only from the mother. In this regard, it is different from nuclear DNA that consists of genetic material from both parents. mtDNA is thought to be a bacterium like organism that had been captured by a cell. It does not have the ability for error checking during replication and is more susceptible to mutations than nuclear DNA. Restriction site differences or the edit distance between two samples can be used as an estimate on how many years ago was the common ancestor alive. Individuals with low edit distances between their mtDNA will have a more recent common ancestor. When humans migrate to a particular region, after a period of time, that region will have many humans with one of the migrated human females as a common ancestor. This common ancestor will be be more recent than the common ancestor for a descendant of one of the migrated humans and a descendant from the original population that did not migrate. mtDNA edit distance can be thus used to induce genealogical trees of the form shown in figure 1. This can lead to an understanding of the origins of populations of certain geographic regions and human
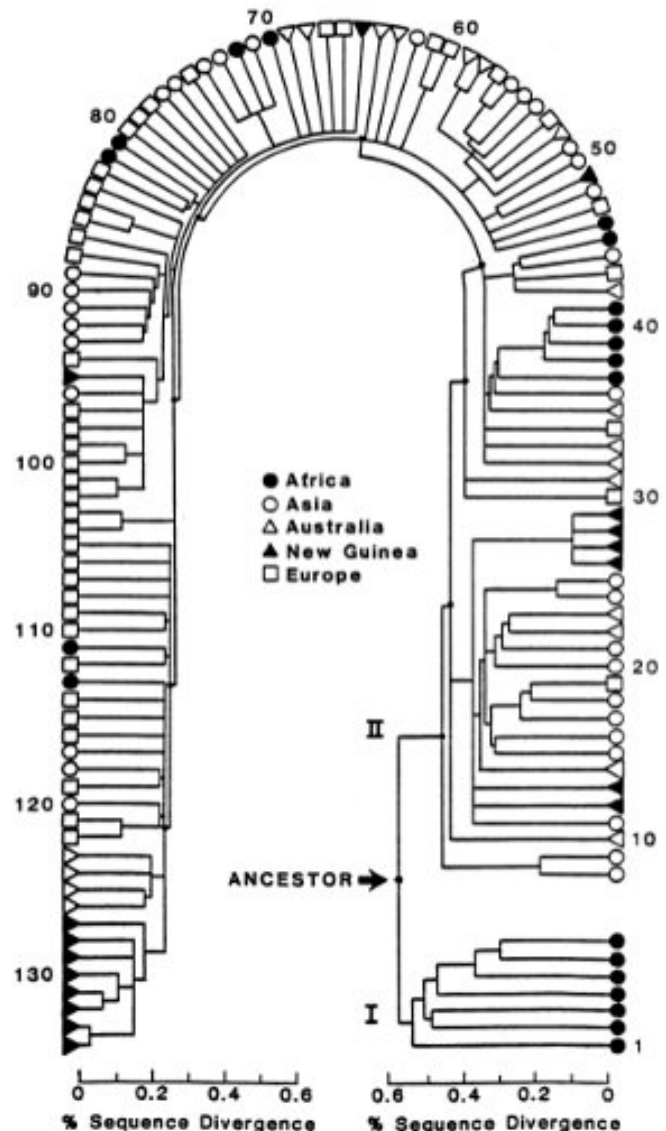

Fig. 1. Human geneological tree based on mtDNA samples [2]

migration paths. The paper written by Cann et. al. suggests that human beings originated in Africa since the common
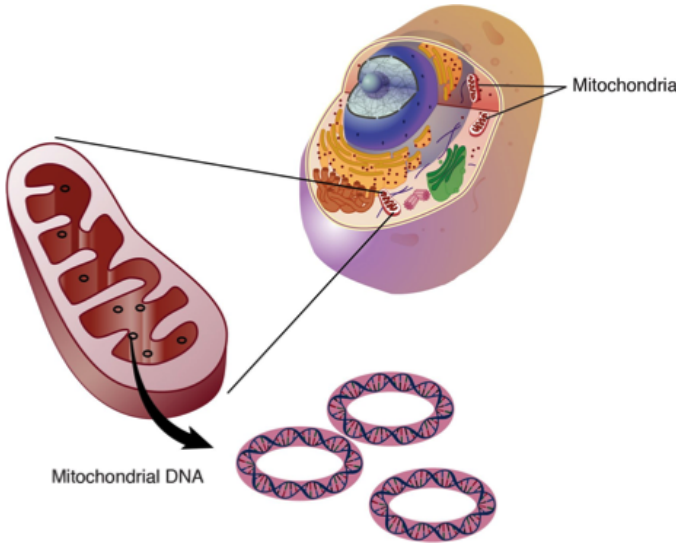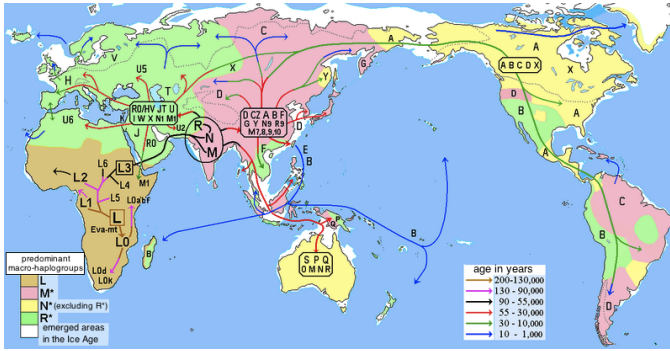
Fig. 2. Mitochondrial DNA[1]

Fig. 3. Human migrations and mitochondrial haplogroups. The letters stand for haplogroups, which are groups of people who share a common ancestor [6].

ancestor shown in figure 1 would need to be African in order to minimize the number of intercontinental migrations needed to account for the geographic distribution of mtDNA types.

The human mtDNA molecular clock is the rate at which mutations have been accumulating in the mitochondrial genome. The mutation rate differs between coding and non-coding regions of the mtDNA. Coding region mutations may be fatal or may lead to other complications and due to rthis reason, mutations in this region will lead to purifying selection. Some studies avoid coding region mutations, while other studies consider both regions and apply a correction factor for selection in coding region.

II. COMPUTER SCIENCE PROBLEM

A. Edit Distance

The edit distance between two mtDNA sequences can be found using Dynamic Programming. Since only the edit distance score is needed, the computation can be done using an array of two columns with the number of rows equal to the length of a mtDNA sequence. For 2699 samples (see figure 4), 3.6 million edit distance computations would need to be done. Even with C++, this amount of computation would take too long to execute. In order to complete the project, a subset of the samples was used. A penalty of 1 was used for insertion, deletion and substitution during edit distance computation.

B. Clustering

The evolutionary tree would need to be found out by running clustering on the mtDNA samples using the edit distance as the input to clustering. mtDNA samples with smaller edit distances would form clusters. These would be clusters corresponding to leaves of the evolutionary tree with a common ancestor. The clusters would then be combined based on the distance between the cluster centroids. This would give us common ancestors of the initial clusters. The process would be repeated till we find a common ancestor for all the mtDNA samples.

The Unweighted Pair Group Method with Arithmetic Mean (UPGMA) algorithm [5] was used for heirarchical clustering of mtDNA samples. The length of an edge between two clusters will be the difference in heights between them and will be a measure of their separation in years. Given two clusters C_1 and C_2, the UPGMA algorithm defines the distance between them to be the average pairwise distance:

$$D(C_1, C_2) = \frac{1}{|C_1||C_2|} \sum_{i \epsilon C_1} \sum_{j \epsilon C_2} D(i,j)$$

Algorithm 1 shows the details of the algorithm and it is called with parameters D, the edit distance matrix and n the number of elements.

Algorithm 1 UPGMA Algorithm

1: **procedure** UPGMAALGORITHM.$UPGMA(D, n)$
2:    Form n clusters, each with a single element
3:    Construct graph T by assigning isolated vertex to each cluster
4:    Assign height $h(v) = 0$ to every vertex v in graph
5:    **while** there is more than one cluster **do**
6:       Find two closest clusters C_1 and C_2
7:       Merge C_1 and C_2 into a new cluster C with $|C_1|+|C_2|$ elements
8:       **for** every cluster $C^* \neq C$ **do**
9:          $D(C, C^*) = \frac{1}{|C||C^*|} \sum_{i \epsilon C} \sum_{j \epsilon C^*} D(i,j)$
10:       **end for**
11:       Add a new vertex C to T and connect to vertices C_1 and C_2
12:       Vertex height $h(C) = \frac{D(C_1, C_2)}{2}$
13:       Assign length $h(C) - h(C_1)$ to the edge (C_1, C)
14:       Assign length $h(C) - h(C_2)$ to the edge (C_2, C)
15:       Remove rows and columns of D corresponding to C_1 and C_2
16:       Add a row and column to D for the new cluster C
17:    **end while**
18:    return T
19: **end procedure**

Area	Samples
Africa	287
North America	11
South America	14
Asia	922
Australia	34
Europe	1192
Melanesia	56
Micronesia	4
Middle East	45
Polynesia	9
South Asia	125
Total	**2699**

Fig. 4. Number of mtDNA samples from each geographic regions
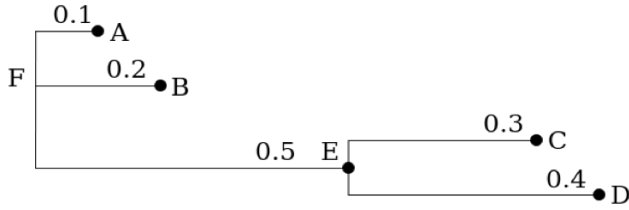
Fig. 5. Newick format illustration [7] .

Fig. 6. Africa Phylogenetic Tree

III. TASKS

A. Download mtDNA sequences

A subset of the 2699 mtDNA sequences was downloaded into text files from the Human Mitochondrial Genome Database [4].

B. Compute Edit Distance Matrix

The edit distance matrix for the subset of the samples was be computed by finding out the edit distance using all possible pairs of mtDNA.

C. Clustering and Evolutionary Tree

Clustering was done using the UPGMA (Unweighted Pair Group Method with Arithmetic Mean) clustering algorithm as described in [5] in order to create an evolutionary tree.

D. Evolutionary Tree Illustration

A script for showing the evolutionary tree was generated during clustering. The script was generated in the Newick format [7]. An example of this format is shown in figure 5. Nested parentheses are used for specifying heirarchy where node name is followed by colon and node height. An the Newick format script for the tree shown in figure 5 is $(A : 0.1, B : 0.2, (C : 0.3, D : 0.4) : 0.5)$.
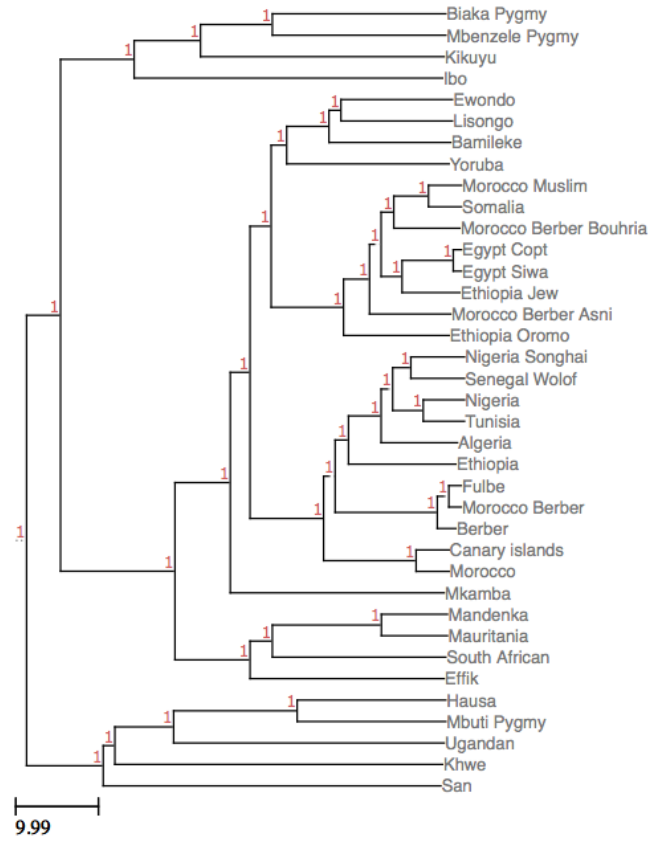
IV. RESULTS

A. Africa Evolutionary Tree

The tree is shown in figure 6. We can see that groups with large separation (with a less recent common ancestor) are all from sub-saharan Africa. They appear to be the humans whose common ancestor is Mitochondrial Eve. People who live near to each other appear to have a more recent common ancestor like in the case of Morocco and Canary Islands

B. South Asia and Middle East Evolutionary Tree

The tree is shown in figure 7. Mainland Indians (figure 8) are closer to Onges (figure 9) than they are to Iraqis (figure 10). Outward features are thought to be a more recent development from around 50,000 years ago [5] and these cannot be used a guide to gauge the closeness of relations between peoples.
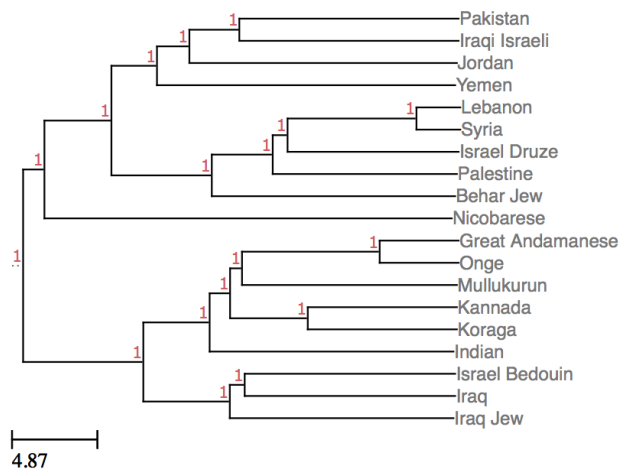
Fig. 7. South Asia and Middle East Phylogenetic Tree

Fig. 8. Kal Penn - Actor of Gujrati Indian ethnicity

Fig. 10. Nouri Al-Maliki - ex Prime Minister of Iraq
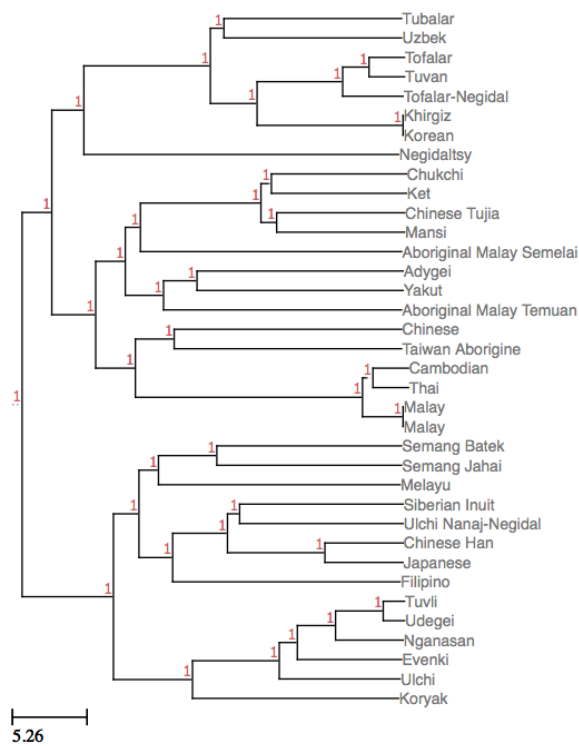

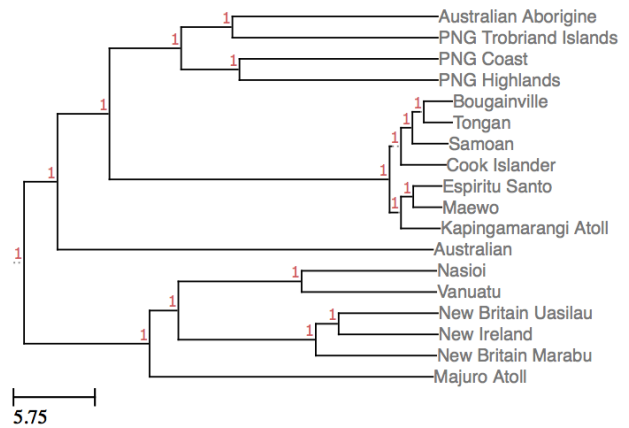Fig. 9. Woman of Onge Indian ethnicity

Fig. 11. Asia Phylogenetic Tree

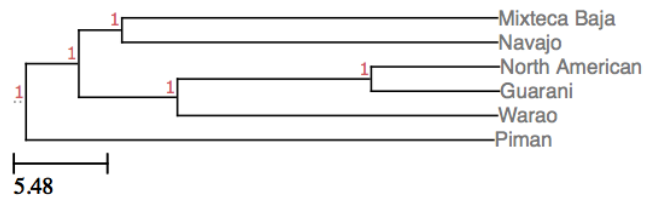Fig. 13. Oceania and Pacific Islands Evolutionary Tree

Fig. 14. North and South America Phylogenetic Tree

D. *Europe Evolutionary Tree*

E. *Oceania and Pacific Islands Evolutionary Tree*

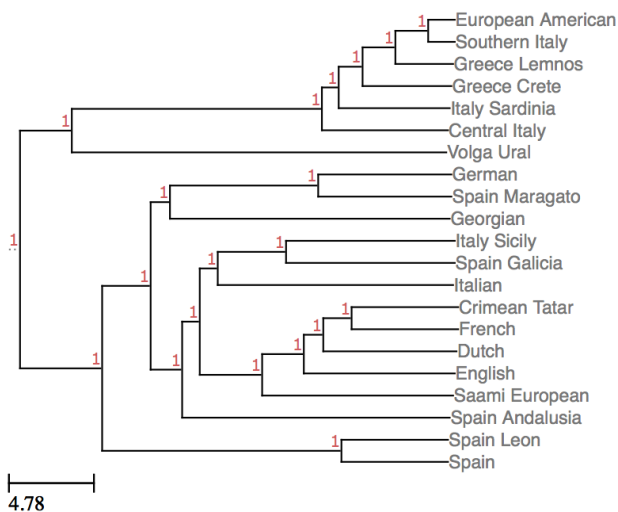F. *North and South America Evolutionary Tree*

G. *World Evolutionary Tree*

Fig. 12. Europe Phylogenetic Tree

C. *Asia Evolutionary Tree*

The tree is shown in figure 11. Japanese and Han Chinese are very closely related. However their culture and customs are very different. Khirgiz and Korean mtDNA samples were identical and this is the reason these two sample show a very recent common ancestor.
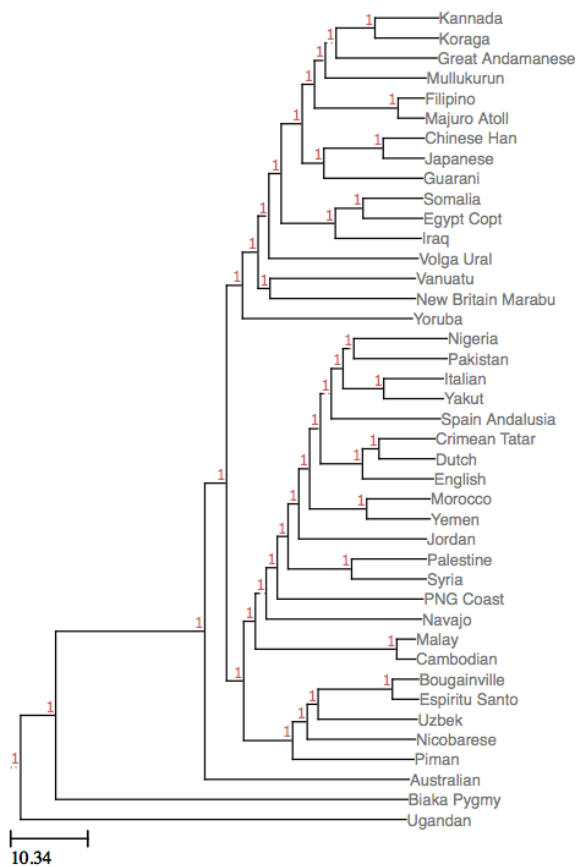
Fig. 15. Abridged World Phylogenetic Tree

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