A mitochondrial DNA-based computational model of the spread of human populations

Peter Revesz
University of Nebraska - Lincoln, prevesz1@unl.edu
A Mitochondrial DNA-Based Computational Model of the Spread of Human Populations

Peter Z. Revesz

Abstract— This paper presents a mitochondrial DNA-based computational model of the spread of human populations. The computation model is based on a new measure of the relatedness of two populations that may be both heterogeneous in terms of their set of mtDNA haplogroups. The measure gives an exponentially increasing weight for the similarity of two haplogroups with the number of levels shared in the mtDNA classification tree. In an experiment, the computational model is applied to the study of the relatedness of seven human populations ranging from the Neolithic through the Bronze Age to the present. The human populations included in the computational study are the Andronovo, the Bell Beaker, the medieval Hungarian, the Khanty, the Minoan, the Rössen and the Únětic populations.

Keywords—Evolution, Mitochondrial DNA, Population Genetics, Similarity Measure, Phylogenetic Tree.

I. INTRODUCTION

Recent advances in biotechnology enable the extraction of ancient mitochondrial DNA (mtDNA) from human bones going back thousands of years. These advances already facilitated several studies of the origin and spread of various mtDNA types, called haplogroups. However, most human populations are highly heterogeneous in terms of their mtDNA haplogroup compositions. Hence even with the newly available mtDNA information, it is not obvious how human populations spread geographically over time. In particular, there are two main challenges for such studies.

The first challenge in studying the relationships among human populations is to develop an easy-to-compute and flexible similarity measure between pairs of human populations based on mtDNA samples from those two populations. Flexibility in this case means that the similarity measure has to accommodate mtDNA haplogroups that are defined to an arbitrary depth or level. For example, we need to be able to compare a relatively short haplogroup description, such as H5 with a long haplogroup description, such as H1a5b2. We define in Equation (2) below for any pair of populations an overall similarity measure that is both easy-to-compute and flexible.

Once a pairwise overall similarity measure is defined, it is possible to build a similarity matrix for all the populations for which mtDNA sample data is available. The second challenge is making valid inferences from the similarity matrix regarding the mutual interaction and spread of human populations. In the area of phylogenetics, which is the study of biological phyla, similarity matrices are used to derive a hypothetical evolutionary tree of the phyla [1]-[3], [5]. However, the algorithms that build hypothetical evolutionary trees, such as Neighbor Joining [10], UPGMA [12] and the common mutations similarity matrix (CMSM) algorithm [6] may not be applicable to the study of human populations for several reasons. First, the time scale of phyla evolution is vast compared to the time scale of the development of human populations. The evolution of biological phyla may take millions of years [11], [14], while ancient human mtDNA samples do not go back more than about ten thousand years. Second, while biological phyla diverge from each other in genetic isolation, when human populations come in contact with each other, they tend to merge their genetic pool. Therefore, the set of mtDNAs in a human population may come from several different ancestor human populations that were each more homogeneous in their mtDNA compositions. In general, if P1 and P2 are two human populations with set of mtDNAs $S_1$ and $S_2$, respectively, such that the condition

$$ S_1 \subseteq S_2 $$

holds, then P1 can be assumed to be an ancestor of P2. However, the reverse is not true. In other words, P1 may be an ancestor of P2 but the above condition may not hold because either not all mtDNAs were transferred from P1 to P2 or some of the transferred mtDNAs have evolved to a different form.

This paper is organized as follows. Section II describes our data collection sources of mtDNA samples from seven human populations. We point out some refinements and revisions of the mtDNA classifications that were given by earlier researchers. We give several mtDNA evolutionary tree figures that show the validity of these refinements. Section III presents a computational model of the overall similarity between two populations based on mitochondrial DNA haplogroup samples from the two populations. Section IV describes experimental results based on seven different populations ranging from ancient Neolithic and Bronze Age European populations to native Siberian tribal populations. Our experimental study reveals which populations are closer or more distantly related with each other. Section V gives a discussion of the results, including a hypothesis of language relatedness of these populations. Finally, Section IV gives some conclusions and directions for future work.
Fig. 1 The phylogenetic tree showing H5 relationships for the following samples: a Bell Beaker containing 4336C 513A 15884A (H5a3), a Khanty containing 16304 93 (H5a3a1), and a Minoan containing 16304C (H5), and another Minoan containing 16172C, which is assumed to be (H5a1g), although other classifications are also possible.
Fig. 2 The phylogenetic tree showing T2b relationships for the following samples: a Hungarian containing 16304C 16218T (T2b6b), a Minoan containing 16304C (T2b), and an Únětice containing 16304C 16292T (T2b3a).
Fig. 3 The phylogenetic tree showing U5 relationships for the following samples: an Andronovo containing 16192T 16270T 16256T (U5a reported as U5a1), a Bell Beaker containing 16270T 16256T 16192C 152C (U5a1a1), another Bell Beaker containing 16192T 16270T 16256T 16114A 16294T (U5a2a), a Hungarian containing 16192T 16270T 16256T 16114A 16294T (U5a2a), a Khanty containing 16270 16256 16239 (U5a1h), a Minoan containing 16192T 16270T 16256T 16311C (U5a1f1), and an Únětice containing 16192T 16270T 16256T 16399G 16222T (U5a1f2). The middle of the figure is cut out because of space limitations.
Fig. 4 The phylogenetic tree showing a U8b relationships for the following samples: an Andronovo 16224C 16311C (U8bK), a Bell Beaker containing 16224C 16311C 16093C 195C (U8bK1a4a1a), a Khanty containing 16224 16311 146 (U8bK1a4a1a1a2b) and a Minoan containing 10550G 11299C 16224C 16311C (U8bK) mutations. The middle of the figure where the options of K1a2 and K1a3 are described is cut out because of space limitations.
II. DATA COLLECTION

The degree of relatedness between two individuals can be estimated based on a comparison of their mtDNA haplogroups. In this paper, we use the mtDNA haplogroup classification provided by PhyloTree.org at http://www.phylotree.org.

Most European mtDNA haplogroups can be classified as belonging to the H, the T and the U haplogroups. According to recent ancient mtDNA data, the U haplogroup is oldest of these three haplogroups to appear in Europe and was followed by the H and then by T haplogroups. These three main mtDNA haplogroups are mixed in all European populations.

A. Sample Populations

We obtained mtDNA data from seven populations with six of them obtained from the ancient mtDNA database website http://suyun.info/index.php?p=ancientdna, which lists the source and age of the samples and classifies them according to cultural groupings. From that database, we selected the following six ancient populations. In order to compare the six ancient populations with an extant population, we also included mtDNA samples from the Khanty, a small native tribe near the Ob River in Siberia. The Khanty appear to be one of the original native people of Eurasia and preserved until recently their traditional hunting and gathering lifestyle. Hence the seven populations selected can be listed as follows:

1. Andronovo: The Andronovo culture, which is noted for the domestication of horses and burial in kurgans, flourished in the steppe region to the north and the east of the Caspian Sea in today’s Kazakhstan and Russia [15]. The database contains nine Andronovo mtDNA samples dated 1800 – 1400 BC. The mtDNA samples in the ancient mtDNA database website are:

   Andronovo = \{H6, T1a, T2a1b1, U2e2, U4, U5a1, U8bK2b, Z1\}

   Some of the haplogroup classifications are outdated because of changes in the mtDNA classification tree. We highlight in this paper in blue any updates made based on the most recent version of the PhyloTree.org mtDNA classification (February 19, 2014).

2. Bell Beaker: The Bell Beaker culture is a prehistoric Western European culture that was named after its characteristic bell-shaped pottery [16]. Some megalithic structures, for example, Stonehenge is associated with the Bell Beaker culture [16]. The database contains eighteen Bell Beaker mtDNA samples dated 2600 – 2050 BC.

   Bell_Beaker = \{H, H, H1, H1e7, H3, H3b, H4a1, H5a3, H13a1a2c, I1a, J, T1a, U2e2, U4, U5a1, U5a2a, U8bK1a4a1a, W5a\}.

3. Hungarian: The ancient DNA website contains mtDNA data from around 1000 AD. This is the most ancient available data regarding the Hungarian cultural group. The data contains the following 28 samples based mostly on [13].

   Hungarian = \{H, H, H, H, H5, H5, HV, I, M, N1a, N1a, N9a, R, R, T, T, T2b, T2b, U, U3, U4, U4, U4, U5a2a, V, X, X\}.

4. Khanty: This is a native tribe of North Siberia. The 106 samples given by [4] are listed below where a superscript denotes the frequency of occurrence:

   Khanty = \{A1, C^5, C^5, D^{17}, F1c, G2a^2, H^{14}, H5a3a1, J1e^4, J1b1^8, J2b^4, N1a, T, T1, T1a1^3, U1b, U2e2, U4^9, U5a^5, U5a1, U7a^{15}, U8bK1a4a1a2b\}.

5. Minoan: The Minoan culture, noted for building the ancient palace of Knossos, flourished on Crete, Santorini and some other Aegean islands [17]. The database contains 34 Minoan mtDNA samples dated 2400 – 1700 BC.


   The PhyloTree.org classification tree changed slightly since the Minoan study was done. For example, in the latest version the classifications T3 and T5 are now placed within the T2 branch. The update from H to H5 is possible because of the mutation 16304C. We also expanded one U5a into a U5a1f1 and though the expansion to U5a2e is also theoretically possible because both of these contain the 16311C mutation.

6. Rössen: The Rössen culture is a Neolithic Central European culture that built settlements consisting of trapezoidal or boat-shaped long houses [18]. The database contains ten mtDNA samples dated 4625 – 4250 BC.

   Rössen = \{H1, H5b, H16, H89, HV0, U8bK, N1a1a, T2, T2e, X2\}.

7. Únětice: The Únětice culture is a Bronze Age culture with sites known from Central Germany, the Czech Republic and Slovakia [19]. The Únětice culture is noted for the Nebra Sky disk and other metal artifacts [17]. The database contains twenty mtDNA samples dated 2200 – 1800 BC.

   Únětice = \{H11a, H2a1a3, H82a, H4a1a1a5, H3, H7h, I, I1, T1, T2, T2, T2b, U, U2, U5a1, U5a1f2, U5b, W, X\}.
B. Examples of Haplogroup Similarities

The haplogroups given by researchers can be often refined using the researchers’ own published mutation observations and the most recent PhyloTree.org classification. The refinements are important to make more precise comparisons among the studied populations. Below we show examples of some of the interesting findings.

C. The H5 Haplogroup

Fig. 1 shows the findings within the H5 haplogroup, involve some refinements. Fig. 1 is composed of a small part of the PhyloTree.org classification tree in the yellow region together with our annotations on the right. We use this method of illustration for two reasons. First, it avoids unnecessary typing errors. Second, the readers can check what was the status of the classification tree at the time of this study. Therefore, future updates of the haplogroup classifications can be made easier because attention can be focused on the parts that changed.

Fig. 1 shows that there is a H5a3 Bell Beaker, an H5a3a1 Khanty, and an H5a1g Minoan sample in the database.

D. The T2b Haplogroup

Fig. 2 shows that there is a Hungarian, a Minoan and an Únětice sample that falls within this haplogroup.

E. The U5 Haplogroup

Fig. 3 shows that Bell Beaker 1, Khanty, Minoan and Únětice samples share the U5a1 haplogroup. Even more remarkably, the Minoan and the Únětice samples share the U5a1f haplogroup. Finally, Bell Beaker 2 and Hungarian share the U5a2a haplogroup.

F. The U8b Haplogroup

Fig. 4 shows that Andronovo, Bell Beaker, Khanty and Minoan samples share the U8bK haplogroup. Moreover, the Bell Beaker and the Khanty share the U8bK1a4a1a haplogroup.

Table 1 shows a summary of the major haplogroup findings. The table uses the following legend:

<table>
<thead>
<tr>
<th>B</th>
<th>H</th>
<th>K</th>
<th>M</th>
<th>R</th>
<th>U</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>T1a</td>
<td>U2e2</td>
<td>U5a</td>
<td>U8bK</td>
<td>U5a1</td>
</tr>
<tr>
<td>B</td>
<td>U5a2a</td>
<td>H5a3</td>
<td>T1a</td>
<td>U8bK</td>
<td>U8bK</td>
</tr>
<tr>
<td>C</td>
<td>T2b</td>
<td>U5a</td>
<td>U5a1</td>
<td>U8bK</td>
<td>U5a1</td>
</tr>
<tr>
<td>D</td>
<td>H5a1</td>
<td>U13a1a</td>
<td>T1a</td>
<td>U5a1</td>
<td>U8bK</td>
</tr>
<tr>
<td>E</td>
<td>U8bK</td>
<td>H4a1</td>
<td>U5a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>T2e</td>
<td>U8bK</td>
<td>U5a1f</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

III. A COMPUTATIONAL MODEL

We say that a level 1 relationship exists between two individuals if they belong to the same haplogroup (single capital letter) but do not share further classifications. We say that a level 2 relationship exists between two individuals if they belong to the same sub-haplogroup (capital letter and number) but do not share further classifications. In general, we say that a level n relationship exists between two individuals if their haplogroup classifications share the first n elements. For example, H1a2 and H1a5b have a level 3 relationship because they share H1a, that is, three elements, namely the haplogroup H, the sub-haplogroup H1 and the sub-sub-haplogroup H1a.

Note that the largest shared level is a unique number for any pair of haplogroups. This allows us to define the function

\[
\text{Level}(s_1, s_2) = N
\]

which takes as input two haplogroups \( s_1 \) and \( s_2 \) and returns the maximum level numbering of the relationship that exists between them. For example,

\[
\text{Level}(H1a2, H1a5b) = 3.
\]

We also define the weight function

\[
W: N \rightarrow N
\]

which takes as input a level number and returns a weight value. For example, W(3) returns the weight of level 3 relationships. The weight is intended to describe the degree of unusualness of the existence of a relationship. Normally we would expect the weights to increase exponentially in value because the mtDNA haplogroup tree has many branches at all levels.

We define the overall similarity between two bags of
mtDNA samples $S_1$ and $S_2$ by the following equation:

$$sim(S_1, S_2) = \frac{\sum_{a \in S_1, b \in S_2} W(\text{Level}(a, b))}{n \times m}$$  \hspace{1cm} (2)

where $n$ and $m$ are the number of samples in the two bags. Since $S_1$ and $S_2$ are bags (instead of sets), they can contain repetitions. Equation (2) says that the similarity of $S_1$ and $S_2$ equals to the weighted sum of the relationships between pairs of individuals from $S_1$ and $S_2$ divided by the total number of possible pairs. Overall similarity measures closely related to symmetric relation. Hence

$$sim(S_1, S_2) = sim(S_2, S_1)$$  \hspace{1cm} (3)

Equation (2) could be further refined if we would know precisely the probabilities of each haplogroup because then we could select the weight function to return for each level a value that is in inverse proportion to the probability that two random haplogroup samples have the given level of relationship.

Although Equation (2) could be improved with more statistical information, it is a good first approximation of the overall similarity between two populations. For simplicity, in this paper we assume that the weight function is defined as:

$$W(0) = 0$$
$$W(1) = 0$$
$$W(2) = 0$$
$$W(3) = 0$$
$$W(i) = 5^{(i-3)} \text{ for } i \geq 4$$

Using the above weight function we can add to each entry in Table 1 the count for each level three or higher relationship. The result is shown in Table 2. Unêtice

Table 2 Level 4 or higher haplogroup relationships among the seven populations. For each shared haplogroup, frequencies greater than one are indicated by a superscript.

<table>
<thead>
<tr>
<th>B</th>
<th>H</th>
<th>K</th>
<th>M</th>
<th>R</th>
<th>U</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>U2e2</td>
<td>U8bK</td>
<td>U5a1</td>
<td>U8bK</td>
<td>U5a1</td>
</tr>
<tr>
<td>B</td>
<td>U5a2a</td>
<td>H5a3</td>
<td>H13a1a</td>
<td>U8bK</td>
<td>H4a1</td>
</tr>
<tr>
<td>H</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>K</td>
<td>U8bK</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IV. EXPERIMENTAL RESULTS

A. Computation of a Similarity Matrix

Using Equation (2), we computed the similarity matrix for the seven populations as shown in Table 3. Note that the similarity matrix is symmetric because of Equation (3). Each non-diagonal entry of the similarity matrix contains the overall similarity value between two different populations described in the corresponding row and column.

Table 3 Similarity matrix among seven populations.

<table>
<thead>
<tr>
<th>B</th>
<th>H</th>
<th>K</th>
<th>M</th>
<th>R</th>
<th>U</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>.0926</td>
<td>0</td>
<td>.005</td>
<td>.114</td>
<td>.0556</td>
</tr>
<tr>
<td>B</td>
<td>.0496</td>
<td>.095</td>
<td>.098</td>
<td>.0278</td>
<td>.0417</td>
</tr>
<tr>
<td>H</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>K</td>
<td>.00832</td>
<td>.0047</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>.0882</td>
<td>.0368</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

As an example of the calculations in making Table 3, consider the entry for row A and column B. This entry contains the overall similarity between the Andronovo and the Bell Beaker samples. This entry can be calculated by Equation (2) as follows:

$$sim(\text{Andronovo, Bell Beaker}) = \frac{5 + 5 + 5}{9 \times 18} = 0.0926$$

Similarly, the overall similarity between the Bell Beaker and the Minoan populations is:

$$sim(\text{Bell Beaker, Minoan}) = \frac{25 + 5 + 6(5)}{18 \times 34} = 0.098$$

As another example, the overall similarity between the Bell Beaker and the Khanty populations is:

$$sim(\text{Bell Beaker, Khanty}) = \frac{5 + 5 + 7}{18 \times 106} = 0.4095$$

V. DISCUSSION OF THE RESULTS

In general, the higher is the similarity value between two populations, the more closely related those two populations are. According to that intuition, the highest similarity (0.4095) is between the Bell Beaker and the Khanty populations as shown Table 3. The outstanding similarity value is mainly due to the remarkable sharing of the U8bK1a4a1a haplogroup. The close relatedness of these two groups is further confirmed by the presence of two other level four shared haplogroups. This leaves little doubt that the Bell Beaker and the Khanty populations are genetically related.

The next highest similarity is between Andronovo and Minoan (.114), then Bell Beaker and Minoan (.098), then Andronovo and Bell Beaker (.0926), then Minoan and Rösse (0.0882), then Andronovo and Unêtice (.0556), then Bell Beaker and Hungarian (.0496), then Bell Beaker and Hungarian (.0417), and then Minoan and Unêtice (.0368).

Perhaps a deeper insight can be gained from the data if we also consider which haplogroups are the major links (level 3 or higher relationships) between each pair of populations.

Table 1 shows that the Andronovo, Bell Beaker, Khanty and Minoan are related via the T1a haplogroup, the Hungarian,
Minoan and Únětice are related via the T2b haplogroup and the Minoan and the Rössen populations are related via the T2e haplogroup. Fig. 5 illustrates these relationships in a Venn Diagram.

Fig. 5 shows that only Minoan shares all three of the haplogroups T1a, T2b and T2e. None of the other six populations shares even two of these haplogroups. One possible scenario that fits this situation is that the T haplogroup reached Europe via the Eastern Mediterranean. With the diversification of the T haplogroup, various founder populations branched off from the Aegean area. The earliest groups (indicated by purple in Fig. 5) only carried the T1a haplogroup. Later groups that branched off from the same region had T2b (green) and T2e (red) in them. The lack of T1a in these groups may be due to a founder effect where a small number of originators of the green and the red groups had a dominance of T2b and T2e, respectively.

Unfortunately, the mtDNA data does not allow drawing conclusions regarding the language associated with each of the seven populations in this study. However, either gene flows or common genetic origin between pairs of populations raises the chance of similarity of language. Consistent with the scenario outlined above, it is possible that the Eastern Mediterranean is the common root of a language family that was once associated with speaker who belonged to the T mtDNA haplogroup. Possibly the red, green and purple groups indicate not only genetic diversifications but also branches of a language family originating the same area. Minoan may belong to this language family. Further, the Andronovo, the Bell Beaker and the Khanty languages may be one branch of this language family and Hungarian and Únětice may be another branch. Since Hungarian and Khanty are classified into the Ugric branch of the Finno-Ugric languages, the extinct languages may have also belonged to the same language family.

VI. CONCLUSIONS AND FUTURE WORK

In this paper, we defined a measure for the overall similarity between two populations with mtDNA haplogroup samples. The measure can be applied to the study of the dispersal of various populations that are heterogeneous in terms of their mtDNA compositions.

Our mtDNA haplogroup-based population similarity measure could be extended easily to a Y-DNA haplogroup-based population similarity measure. It would be interesting to perform a similar analysis on Y-DNA data for the populations studied in this paper and compare the similarity matrices generated by the mtDNA and the Y-DNA haplogroup-based data. However, ancient Y-DNA data is much harder to obtain than ancient mtDNA data with current technology. Hence such a Y-DNA study may have to wait until further DNA extraction technology improvements.

Another way to extend the research is to study a larger number of populations. We intend to study more ancient populations as well as more currently living populations to gain additional insight into the origin and dispersal of various populations. Considering populations that encompass a broader time scale and a larger geographic area may give a deeper insight into human pre-history.

REFERENCES


Peter Z. Revesz holds a Ph.D. degree in Computer Science from Brown University. He was a postdoctoral fellow at the University of Toronto before joining the University of Nebraska-Lincoln, where he is a professor in the Department of Computer Science and Engineering. Dr. Revesz is an expert in bioinformatics, databases, data mining, and data analytics. He is the author of *Introduction to Databases: From Biological to Spatio-Temporal* (Springer, 2010) and *Introduction to Constraint Databases* (Springer, 2002). Dr. Revesz held visiting appointments at the IBM T. J. Watson Research Center, INRIA, the Max Planck Institute for Computer Science, the University of Athens, the University of Hasselt, the U.S. Air Force Office of Scientific Research and the U.S. Department of State. He is a recipient of an AAAS Science & Technology Policy Fellowship, a J. William Fulbright Scholarship, an Alexander von Humboldt Research Fellowship, a Jefferson Science Fellowship, a National Science Foundation CAREER award, and a “Faculty International Scholar of the Year” award by *Phi Beta Delta*, the Honor Society for International Scholars.