DATE: November 13, 1973

To : Dr. Joshua Lederberg

FROM: L. L. Cavalli-Sforza

Subject: Chronology of research on phylogenetic analysis

Work with Anthony Edwards in Pavia begun.

Three methods—all approximate—for analysis in the case of gene frequencies or anthropometric traits (least squares, minimum path, cluster analysis. All use matrix of distances between population pairs).

1963 Paper at the Hague Genetics Congress.

Anthony and I start on maximum likelihood solution of problems.

1965 Fitch reinvents independently method 1.

Camin and Sokal independently find approximate method for qualitative traits and accept principle that phylogenetic analysis differs from

standard taxometry.

1966 J. Felsenstein proves covariances between populations are proportional to evolutionary time. Starts on maximum likelihood solution.

1970 Anthony proves that full maximum likelihood solution is practically impossible. Gives paper at Royal Statistical Society of London, all big brass of British statistics attending. No useful advice

obtained.

J. Felsenstein publishes iterative maximum likelihood solution

using matrix of distances.

1973 September, I get interested in measuring "treeness", that is how well data are represented by a model of independent evolution. On a problem concerning distribution of non-independent correlation coefficients, I consult with Ingram Olkin. He mentions a formally related problem was solved by a student of Wilks and he himself has

provided an extension designed to solve a psychological testing problem. Ingram gives me references to Wilks, Votaw's papers. On this basis, the problem of estimation of tree parameters and of treeness can be solved by the likelihood ratio criterion (a somewhat different procedure from classical maximum likelihood but almost as widely accepted). It is basic to use matrix of variances and covariances, not of distances. Solution would have been easy since the beginning if the Wilks' paper—a classic, but rarely read in the original even if it is very readable—had been reinterpreted as an example of a tree with all populations splitting at once.

## Some lessons:

- 1) Fundamental papers should be read in the original and not learned from textbooks.
- 2) There is no universal method best for everything.
- One never considers things from sufficiently different angles.