PB HLTH C240D/STAT C245D: Assignment #3

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Maximum likelihood estimation of the ABO blood group allele frequencies using the EM algorithm

The ABO *blood groups* were the first to be discovered and are important in assuring safe blood transfusions (Cf. Landsteiner, 1930 Nobel Prize in Physiology and Medicine, `nobelprize.org/nobel prizes/medicine/laureates/1930` As indicated in Table 1, the ABO blood groups are characterized by the presence or absence of *antigens* on the surface of red blood cells and *antibodies* in serum. The ABO locus has three *alleles*, A, B, and O, leading to $3^2 = 9$ *phased genotypes*, $3 + 3 \times 2/2 = 6$ *unphased genotypes*, and four *phenotypes*, the blood groups **A**, **B**, **AB**, and **O**.

Let $\pi = (\pi_A, \pi_B, \pi_O)$ denote the ABO allele frequencies in a well-defined population of interest. Under the assumption of *Hardy-Weinberg equilibrium* (HWE), the maternal and paternal alleles are independent, i.e., genotype frequencies are products of allele frequencies. Let $Y = (Y_A, Y_B, Y_{AB}, Y_O)$ denote the ABO phenotype counts for a random sample of n individuals from the population of interest.

The objective of this assignment is to apply the EM algorithm to derive maximum likelihood estimates of the ABO allele frequencies for a dataset from the classical article of Clarke et al. (1959). Specifically, consider the following ABO phenotype counts for a sample of $n = 521$ duodenal ulcer patients (Clarke et al., 1959, Table III): $Y_A = 186$, $Y_B = 38$, $Y_{AB} = 13$, and $Y_O = 284$. For simplicity, you may assume that the $n = 521$ patients are a random sample from a well-defined population, with Hardy-Weinberg equilibrium at the ABO locus.

Question 3. Derivation of EM algorithm.

Derive the expectation-maximization algorithm (EM) for maximum likelihood estimation (MLE) of the ABO allele frequencies $\pi = (\pi_A, \pi_B, \pi_O)$, based on ABO phenotype counts from a random sample of n individuals from a well-defined population, with Hardy-Weinberg equilibrium at the ABO locus.

Specifically, define the observed incomplete and unobserved complete data structures, provide the incomplete and complete data log-likelihood functions, supply the main EM Q-function, and derive explicit solutions for the E- and M-steps.

Question 4. Software implementation of EM algorithm.

Write an R function implementing the EM algorithm for maximum likelihood estimation of the ABO allele frequencies $\pi = (\pi_A, \pi_B, \pi_O)$.

Arguments to this function should include: the phenotype counts, starting values for the allele frequencies, stopping criteria; it should return candidate MLE for the allele frequencies and the corresponding value of the observed data log-likelihood.

Question 5. Application of EM algorithm.

Apply the EM algorithm to derive maximum likelihood estimates of the ABO allele frequencies $\pi = (\pi_A, \pi_B, \pi_O)$ for the Clarke et al. (1959) dataset.

Trace the progress of the EM algorithm by providing a table of candidate MLE for the allele frequencies and corresponding values of the observed data log-likelihood at each iteration.

Also provide graphical summaries of these results.

Comment on the EM algorithm's performance in terms of sensitivity to starting values, convergence, and any other features you deem relevant.

Compare the results from your implementation of the EM algorithm to those from one of the R optimization functions (e.g., optim).