Questions on Li and Durbin (2011) *Nature* 475:493-496.

Inference of human population history from individual whole-genome sequences.

1. Before this paper, what was the standard way to infer population history from genetic variation data?

2. What are the major limitations of inferences of population history based on a single sequence? Can these be overcome by studying large numbers of sample at the locus of interest?

3. The "Pairwise Sequentially Markovian Model" (PSMC) approximates the full coalescent process using a Markov process. What are the hidden states? What information is used to deduce these states?

4. When comparing segments of chromosome with a very distance common ancestor, we expect that they will be more different than segments with a recent common ancestor. What other differences do we expect between the two types of segment?

5. The authors state that their method provides information about population history in the interval between ~20,000 years ago and ~3,000,000 years ago. Why is the approach limited in its ability to infer history outside this interval?

6. What are some of the other limitations with the PSMC model that the authors describe in the paper?

7. The authors describe the transition probability between states t and s as:

$$p(t|s) = (1 - e^{\rho t})\, q(t|s) + e^{\rho t}\, \delta(t - s)$$

   Can you identify the main components of the equation?

8. What struck you most about this paper?