CS 229 Project

Local Ancestry Inference in Admixed Populations

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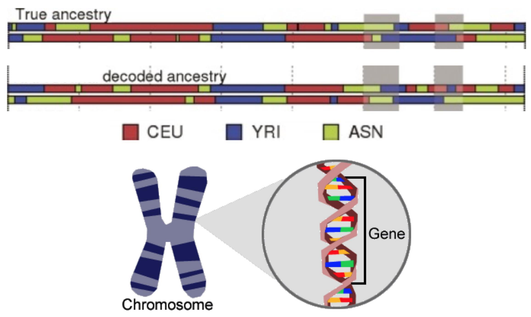
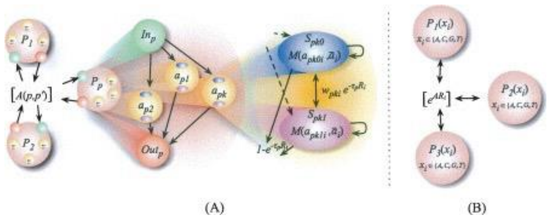
Introduction

Local Ancestry Inference Problem

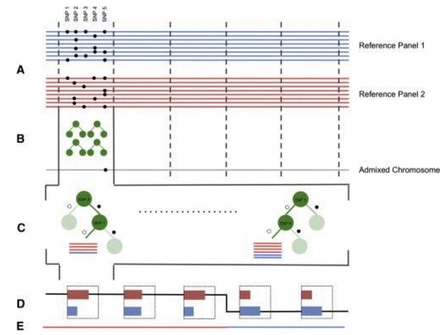


Data:
The 1000 Genomes Projects Phase I – A dataset of 1092 individuals from 14 populations (2013)

HAPAA algorithm:
• Step 1: Divide the genome into continguous windows of SNP's (single neucleotide polymorphisms)
• Step 2: Assign ancestries for genes using a **Hidden Markov Model based** clustering algorithm



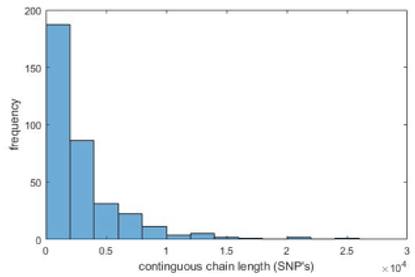
RFMix algorithm:
• Step 1: Segment an input strand of DNA into contiguous windows of SNPs(single nucleotide polymorphisms)
• Step 2: Assign ancestries for genes using a **Conditional random fields (CRF) algorithm** based on randomforests



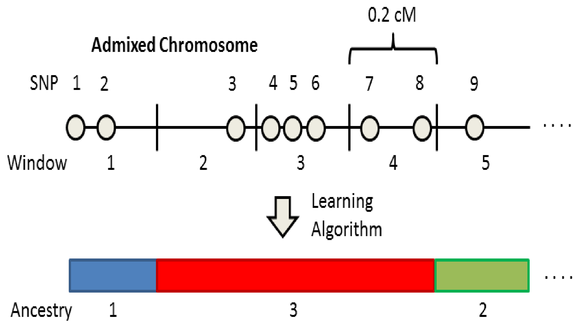
Methods

Data:
• We used pre-processed data that the authors of the RFMix paper provided.
• 51213 SNP's from both chromosome one's of 362 individuals (bi-allelic).
• Test set:10 admixed, Latino individuals, whose genomes were created using a Wright-Fischer simulation to sample 12 generations after admixture.
• The simulated Latino genomes have 45% Native American, 50% European, and 5% African ancestry.
• Training set: 170 Native American, 194 European, and 340 African (Simulated samples were used)

Our scheme:
• Step 1: Segment into windows of fixed size in **centi-morgans**
-The histogram shows distribution of contiguous window sizes in terms of number of SNP's

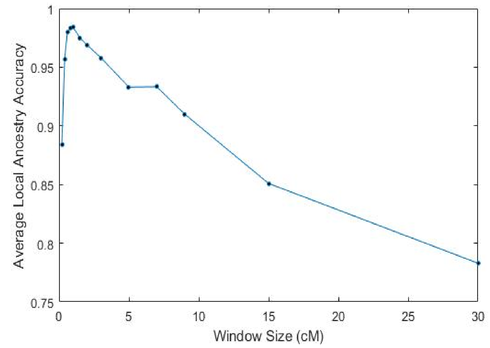


• Step 2: Measure the **Manhattan distances** between the references and thetest sequence in each window
- **Manhattan distance**: counting the number of replacements needed to get rom one window to another.
• Step 3: We then use a voting scheme where the ancestry of the admixed window is assigned the reference population in which it has largest number of to he highest similarity values. (All SNPs in a window are assigned to the same ancestry.)



Results

• By default, using the same test and training set, RFMix uses windows of 0.2 cM and achieves an accuracy of 97.5% averaged over the 10 admixed individuals.



• The results suggest **very high performance**, compared to RFMix, peaking at around 98.4% accuracy for a window size of 1.0 cM.
• For the same window size RFMix uses, of 0.2 cM, the accuracy is 88.4%.
• As window size is increased, the accuracy peaks and then falls rapidly.

Why does ours perform so well?
• We have an extreme abundance of reference panels on which to train in the data set.

What if we only have a small number of references?
• 30 reference(training)examples for each population
Ours: ~97%
RFMix: 95.6%
• 3 reference(training) examples for each population
Ours: 76%
RFMix: 87.8%, 93.2% after one iteration of EM

• RFMix outperforms our simple voting scheme, because of its ability to **construct new reference data from the existing admixed samples**

Way to improve our scheme

• Relax the independence assumptions between the ancestry labels of nearby windows

• Model the recombination process to deal with the few reference panels case

Conclusions

• We seek to better understand how to construct models for local ancestry inference. There are multiple steps forward:

• Reconstructing the recombination process:

- HAPAA utilizes a specific biological model of recombination
- We will construct a model of recombination that allows us simulate more admixed data
- observe how the recombination model affects LAI performance

• Investigate alternative non-biological models of LAI

- We already have created a simple model of LAI using the Manhattan metric that performs well with abundance of training data
- Implement more complex, non-biological HMM based algorithm for sequence recognition
- compare performance of biological with non-biological models
- Implement EM into our non-biological models

Acknowledgement

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Bibliography

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2. Sundquist A, Fratkin E, Do CB, Batzoglou S. Effect of genetic divergence in identifying ancestral origin using HAPAA. Genome Research. 2008;18(4):676-682. doi:10.1101/gr.072850.107.