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Gene genealogies for finding disease-predisposing genetic variants

The gene genealogy describes relationships among sequences sampled from a population. The gene genealogy has been incorporated in approaches to estimate population genetic parameters, like mutation or recombination rates, based on sampled DNA sequences. Knowledge of the underlying genealogy also has potential application in the discovery of disease-predisposing genetic variants. In particular, individuals inheriting the same phenotype-influencing genetic variant are more closely related to each other than individuals not carrying the same variant and they should also share a similar phenotype. We are therefore interested in quantifying the degree to which individuals sharing the same phenotype are clustered in the ancestral tree at the location of the variant that influences the phenotype. In this presentation, I discuss a number of possible statistics for measuring the proximity in the tree of individuals sharing similar phenotype values. I use simulation to show how the proposed statistics can be used to find regions harbouring disease-predisposing variants, with an emphasis on rare genetic variants. Since the true ancestral trees are unknown, I also discuss an approach to sample trees that are compatible with a sample of observed sequences.