Developments in the `snpMatrix` package

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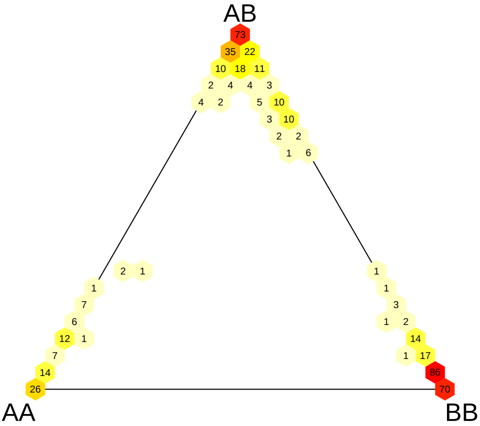
The original aims

- Developed for one of the first GWA studies (WTCCC)
- Implements an efficient storage mechanism for genome-wide SNP data (1 byte per SNP genotype)
- A set of useful statistical tools:
  - LD statistics
  - Single SNP association tests (+ stratification)
  - GLM-based score tests

Recent developments (`snpMatrix2`)

- Extension of storage mechanism to represent *uncertain* genotype assignments
  - Mainly used for *imputed genotypes*, for example using programs such as MACH, IMPUTE (or for storage of internally imputed genotypes)
  - These are represented as posterior probabilities: p_{AA}, p_{AB}, p_{BB}
  - Space divided into 253 regions and still stored as 1-byte RAW variables
- Adaptation of existing statistical methods
- New statistical methods

An uncertain SNP genotype (`plotUncertainty`)



Adapting statistical methods

- `snpMatrix` relies on *score tests*
- Extension to test methods requires replacement of the indicator variables for *additive* and *dominance* effects by their posterior expectations
- Using existing internal imputation methods, we do this “on the fly” without storing the imputed values
- Small changes to every test routine generalizes this to stored uncertain genotypes
- (There has been a small change to the internal imputation method since one method did not give three posterior probabilities)

New and future statistical methods

- In current version:
    - Fast GLM *estimation* routines with SNP genotypes entered either as dependent variable or predictor variables
- Under development:
    - Hypothesis test functions for *multivariate* and *multinomial* phenotypes
    - A fast implementation of the (blockwise) LARS algorithm for variable selection
- Also:
    - Interfaces to read and write data files for the widely-used PLINK toolset