Analysis of genomic markers: Make it easy with the R package MPAgenomics
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Computing the signal-to-noise ratio (SNR) for each profile. Logistic regression is not straightforward to perform the whole analysis. Heavy architecture can be used for CGHcall. For each cluster, choose a calibration method for the segmentation parameter. Choice of the allele B fraction: proportion of total signal from allele B.

Technical biases correction and automatic calibration of huge amount of data can be handled. Assign labels (loss, normal or gain) to segments (copy-number). Provide automatic wrappers of EAS (Easy-to-use Software). Easily build architecture with TumorBoost. Select genomic markers (e.g. SNPs or CNV) associated with a response. Complicated internal documentation is present.

Copy-number analysis
- Technical biases correction
- Copy-number & allele B fraction calculation
- TumorBoost: better allele B fraction correction for studies with matched normal-tumor samples

Difficulties for beginners:
- Complicated internal documentation
- Heavy architecture to deal with
- No way to perform the whole analysis straightforwardly

Segmentation
Copy-number
Copy-number signal is segmented by the PELT segmentation method from changepoint package (Killick et al., 2013).

Allele B fraction
Heterozygous SNPs are kept and the signal is symmetrized. Then, the signal is segmented the same way as the copy-number signal.

Calibration of λ parameter in PELT
- PELT depends on a parameter to calibrate. MPAgenomics: automatic calibration of λ.

Calling method
- Assign labels (loss, normal or gain) to segments (copy-number).
- CGHcall package (van de Wiel et al., 2007).

MPAgenomics contribution
1. Normalize data via MPAgenomics
2. Easily build architecture
3. Provide automatic wrappers of MPAgenomics functions
4. Provide normalized data

Markers selection
Strategy
- Select genomic markers (e.g. SNPs or CNV) associated with a response y.
- Lasso method for sparse selection (few markers) with λ > 0:
  \[ \sum_{i=1}^{n} (y_i - (X\beta)_i)^2 + \rho \sum_{p=1}^{P} |\beta_p| \]

Implementation in MPAgenomics
- Linear regression: HDPenReg for large amount of variables (HDPenReg R package, C++ implementation of LAIS (Efron et al., 2004)).
- Logistic regression: wrapper of glmnet R package (Friedman et al., 2010).
- Choice of λ by k-fold cross validation.

Calibration of λ (segmentation)
- PELT default parameter is misleading.
- MPAgenomics: automatic data-driven choice of λ.

Strategy
1. Grid of λ: 0 < λ_1 < ... < λ_{max}.
2. Run PELT for each λ_i (see Figure 2 left).
3. Choose λ corresponding to the widest range such that the number of segments is constant (> 1).

Sample-specific parameter versus common λ
1. Common λ:
   - Compute the signal-to-noise ratio (SNR) for each profile.
   - Cluster profiles according to SNR (Gaussian mixture).
   - For each cluster, choose λ.
2. Sample-specific λ:
   - MPAgenomics provides an automatic choice of λ for each profile.

Sample-specific parameter versus common λ
Common λ within each cluster is misleading (Figure 2 right).

Bibliography