Bioinformatic challenges associated with ancient DNA

Computational Challenges Workshop
9 November 2015

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at the Mainz Institute of Anthropology

Computational challenges unique to aDNA

- The nature of the question: ascertainment bias and other biases affecting our priors
- The nature of the molecule: biases in preservation and endogeneity unique to aDNA
- The nature of the analysis: biases introduced during NGS and downstream bioinformatics analyses

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Ancient DNA

Modern DNA

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Computational challenges unique to aDNA

- The nature of the question: ascertainment bias and other biases affecting our priors
- The nature of the molecule: biases in preservation and endogeneity unique to aDNA
- The nature of the analysis: biases introduced during NGS and downstream bioinformatics analyses

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Addressing computational challenges unique to aDNA

- The nature of the question: formulate research questions incorporating archaeological and palaeo-population genetic data

- The nature of the molecule: characterize and correct for stereotypical damage patterns

- The nature of the analysis: develop appropriate reference genomic data sets and devise calling and recalibration methods suited to ancient DNA

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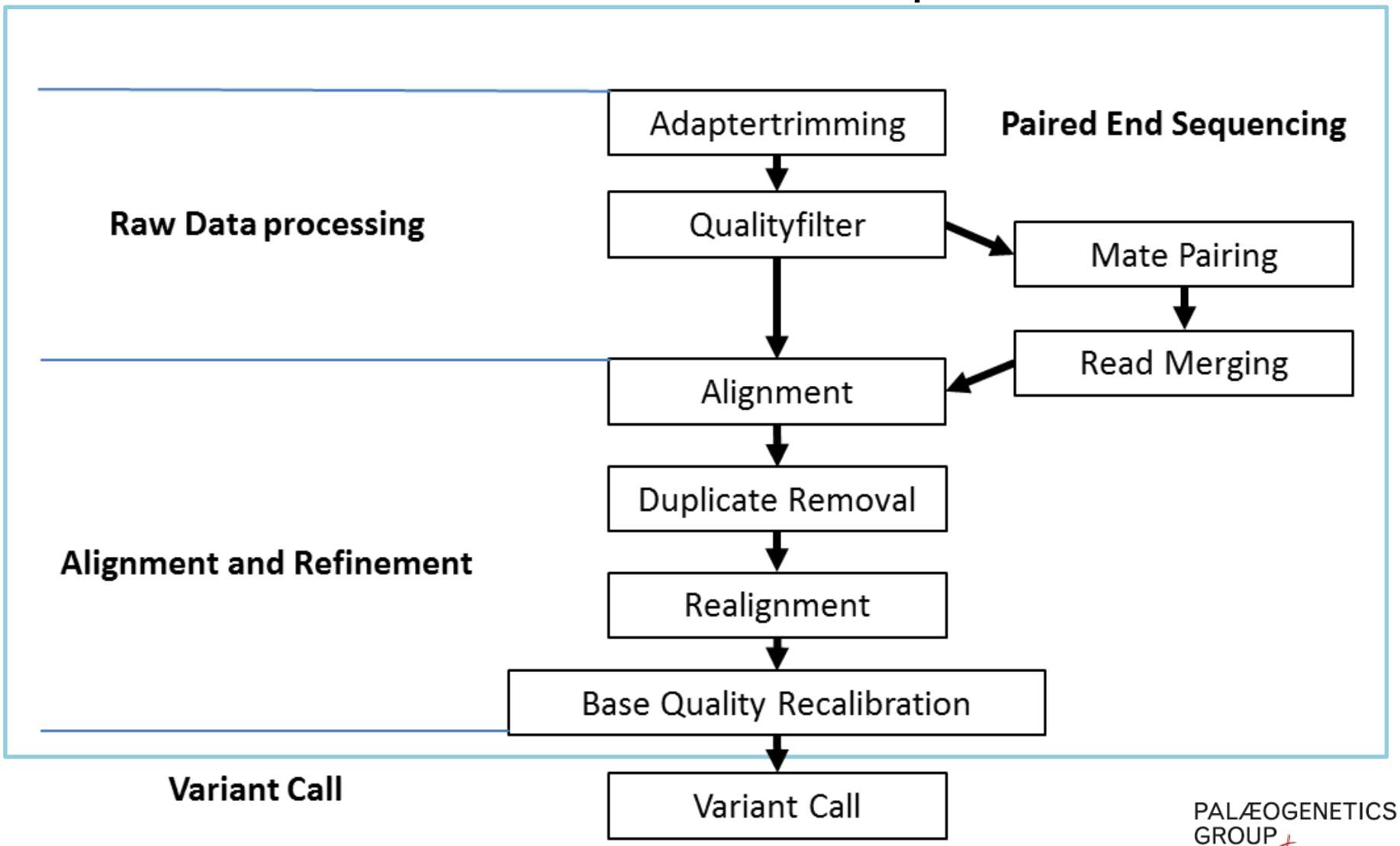
The Bioinformatic Pipeline



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Capturing ancient patterns of genomic variation

= truth

= filtered

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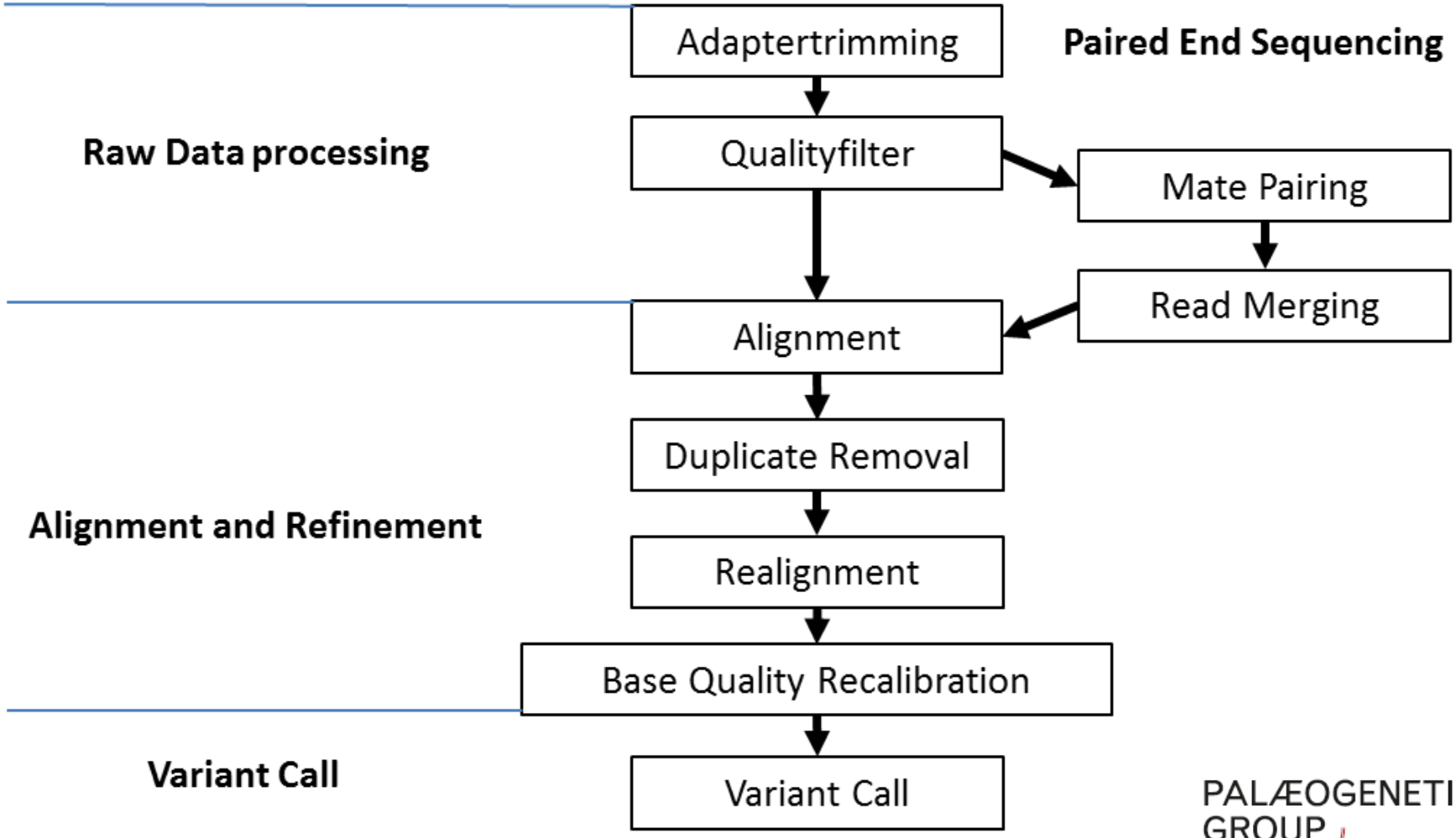
The Bioinformatic Pipeline



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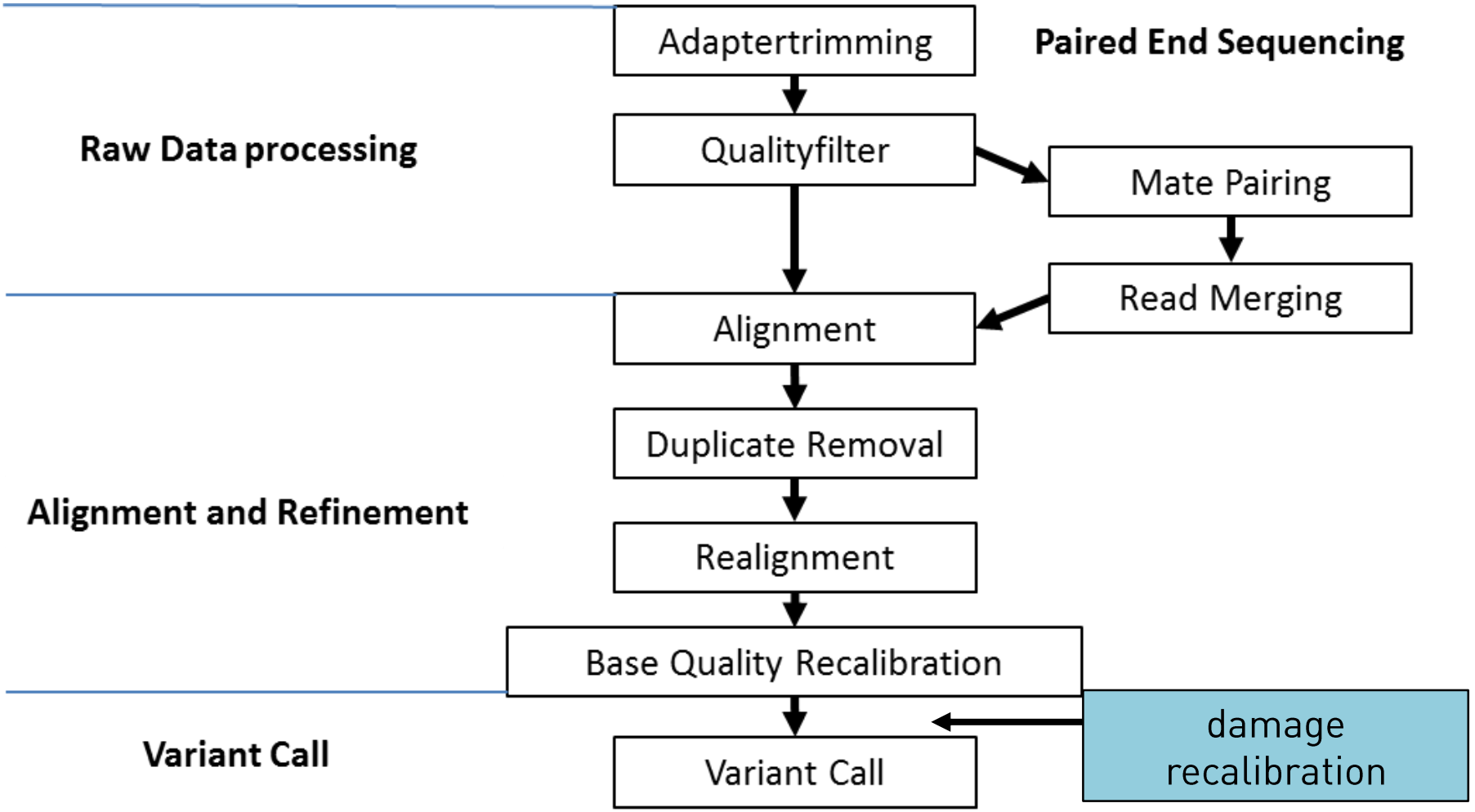
The Bioinformatic Pipeline



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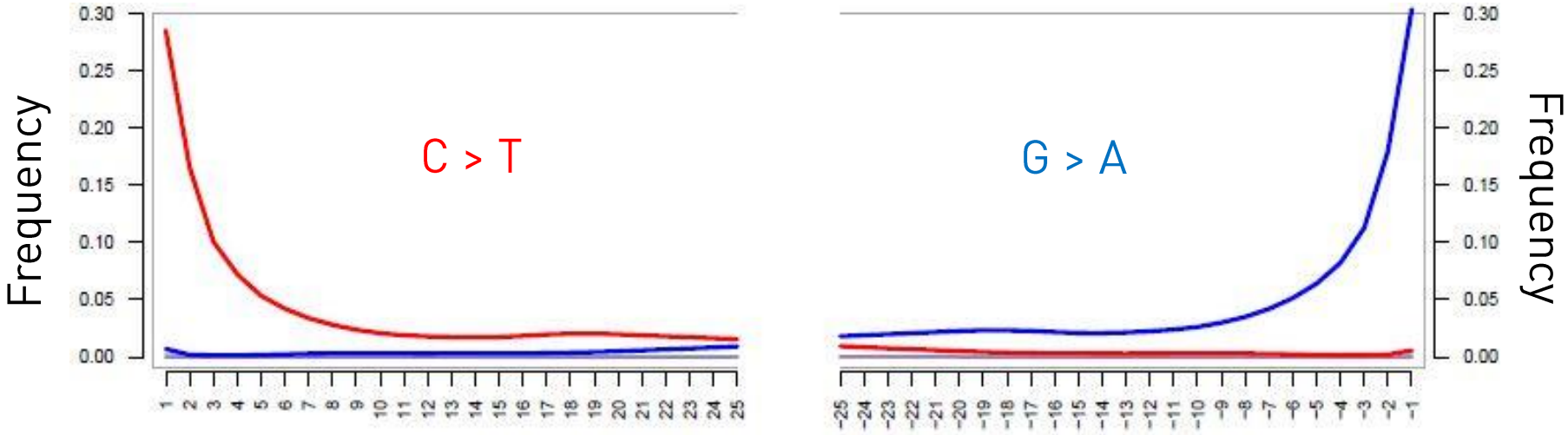
Damage recalibration



Adjust base quality scores in C>T and G>A transitions according to damage patterns, following an empirical model

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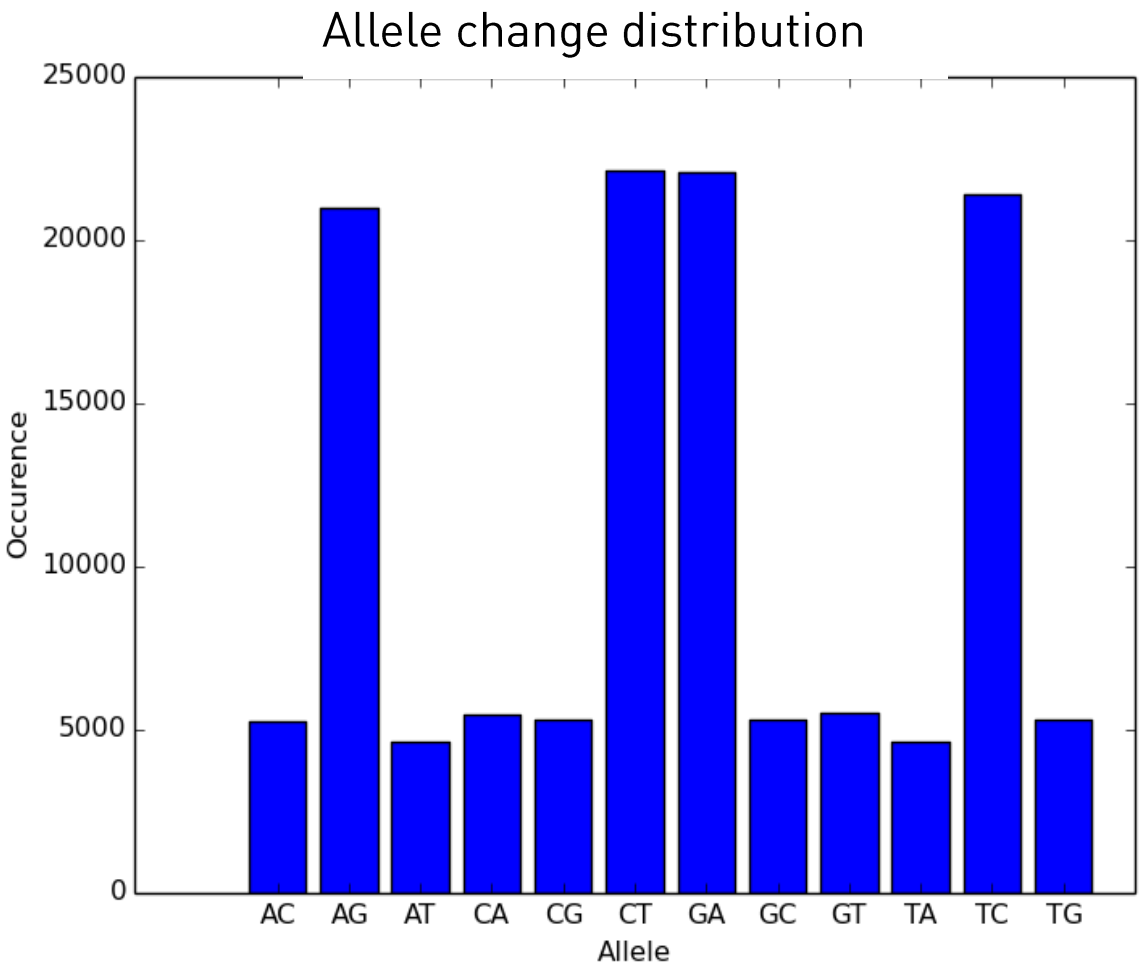
Modern sample NA18534



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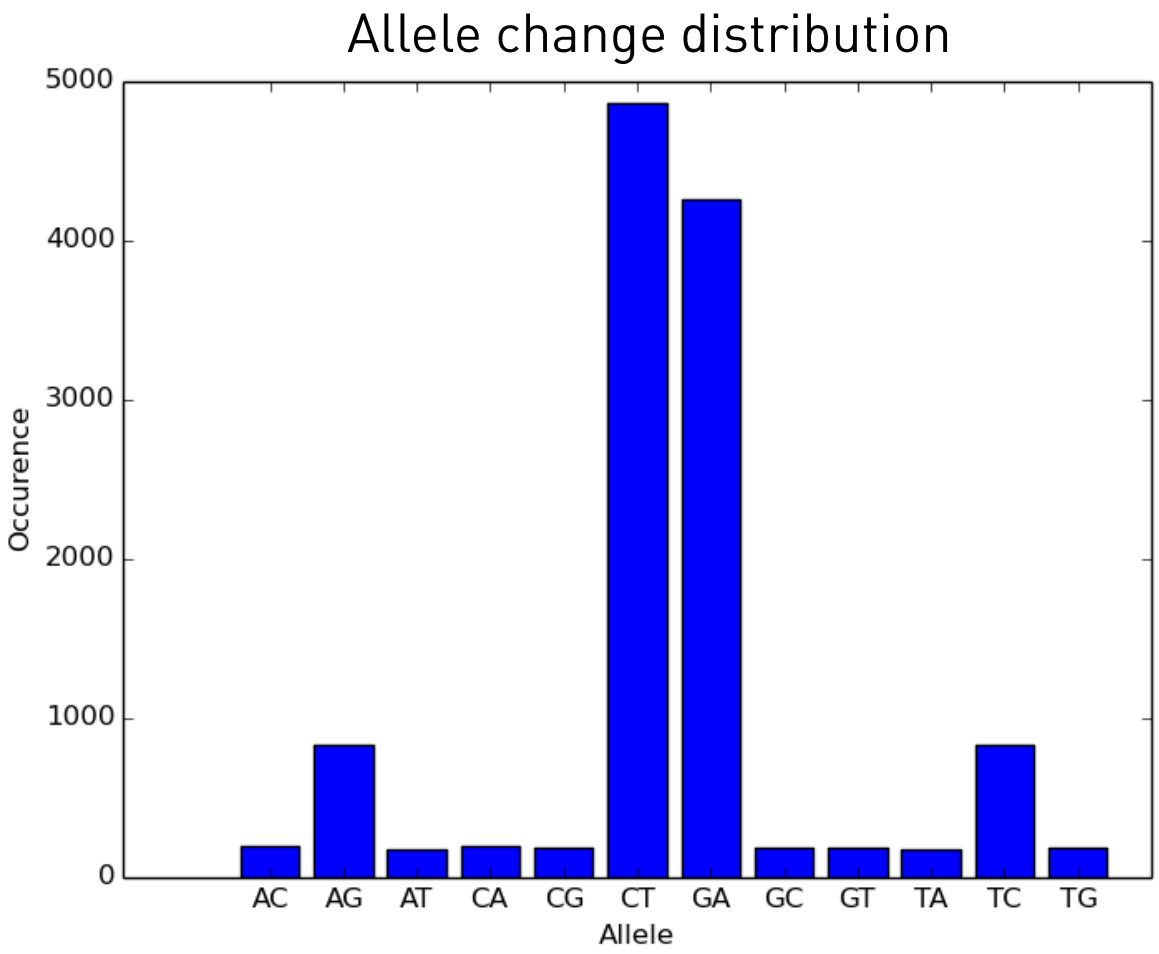
aDNA sample Klei 10



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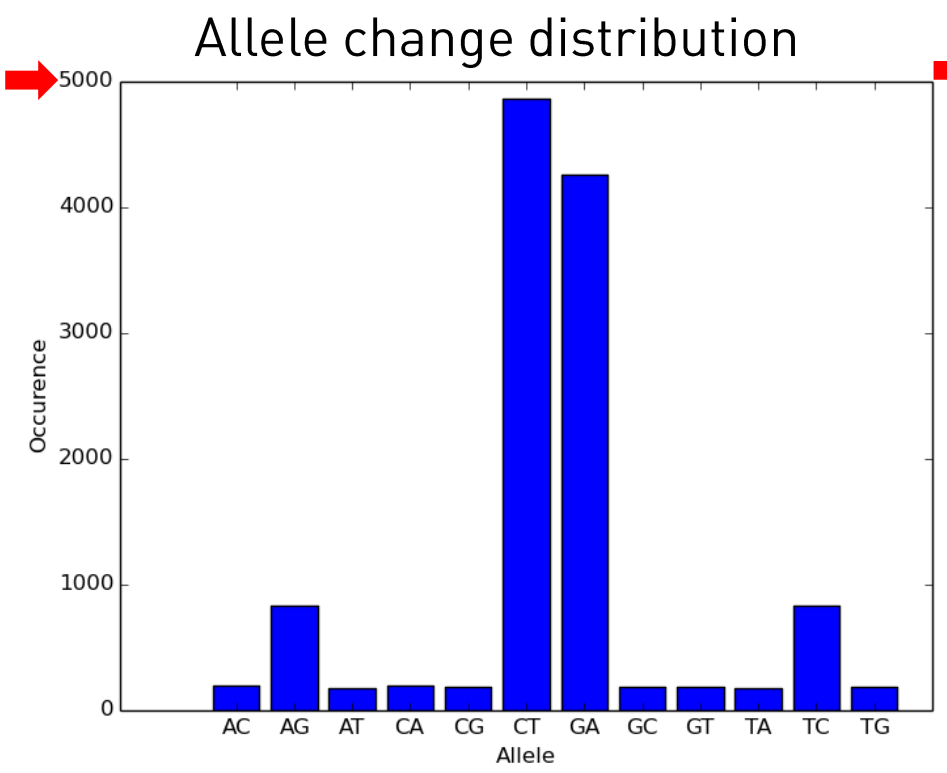
Damage recalibration



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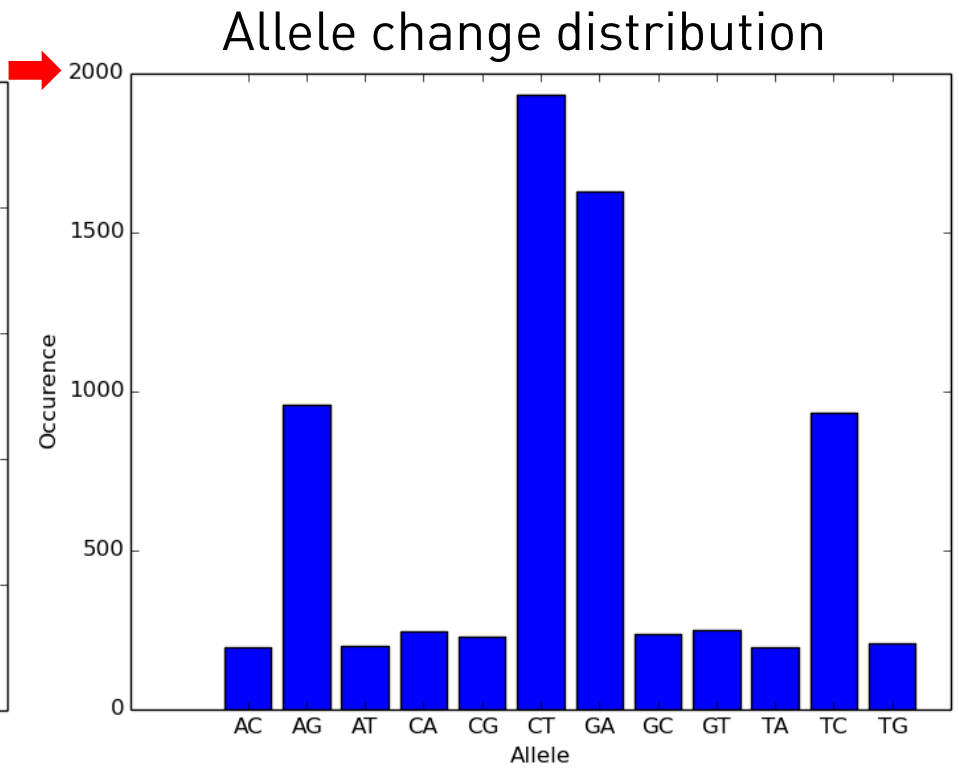

Damage recalibrated

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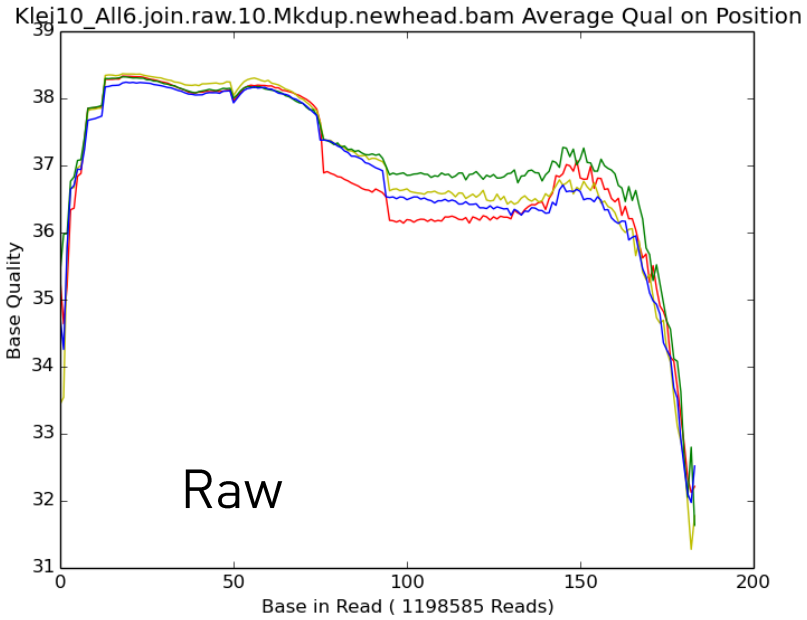
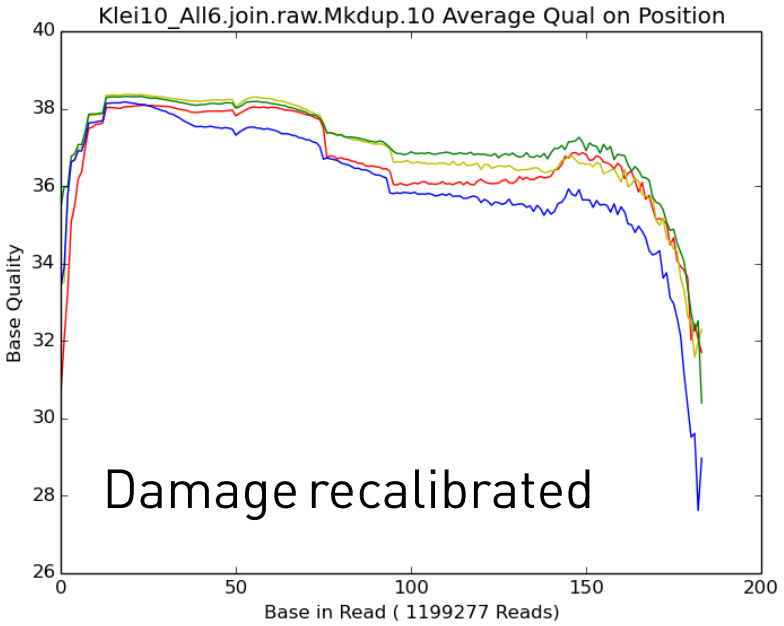
Damage recalibration

Average base quality/position/base



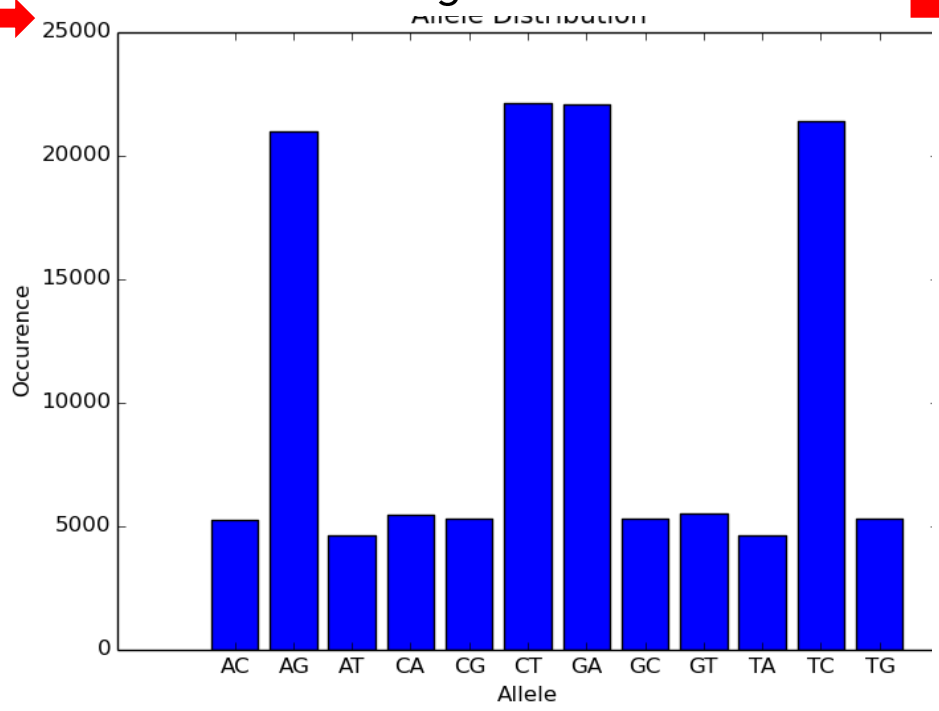


Base	Average	Min	Max
T (red)	36.86	32.13	38.33
STD	3.70	1.50	6.43
A (blue)	36.86	31.98	38.24
STD	3.48	1.69	7.31
C (yellow)	36.94	31.28	38.37
STD	3.30	1.99	7.83
G (green)	36.94	31.28	38.37
STD	3.30	1.99	7.83

Base	Average	Min	Max
T (red)	36.65	30.58	38.09
STD	4.18	2.12	11.81
A (blue)	36.13	27.62	38.17
STD	5.46	2.86	9.78
C (yellow)	36.94	31.58	38.37
STD	3.31	1.55	7.84
G (green)	36.94	31.58	38.37
STD	3.31	1.55	7.84

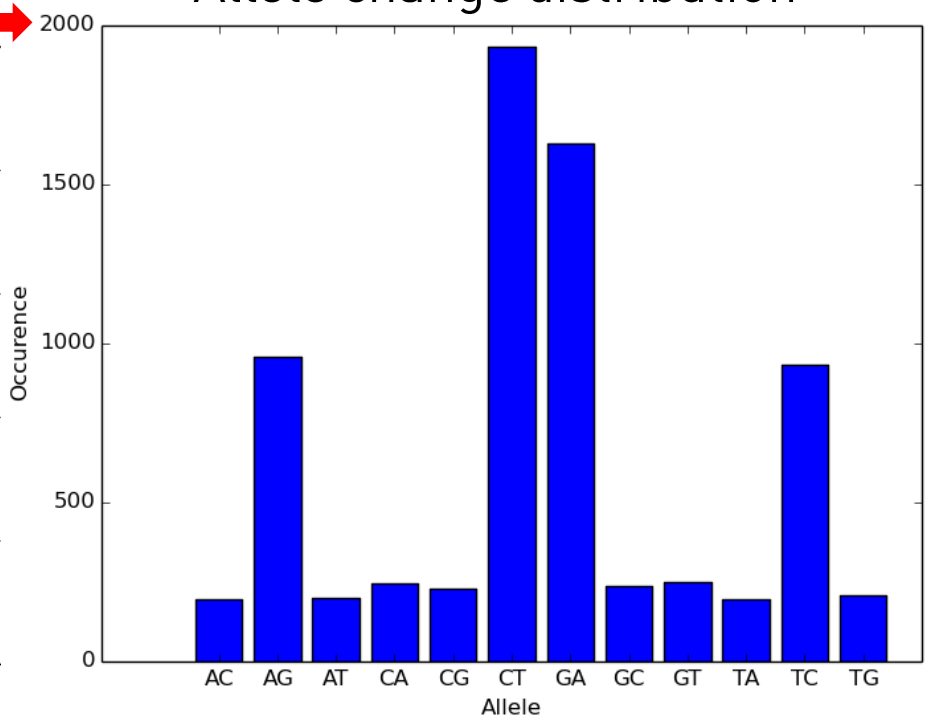
Damage recalibration

Allele change distribution



Modern

Allele change distribution



Damage recalibrated

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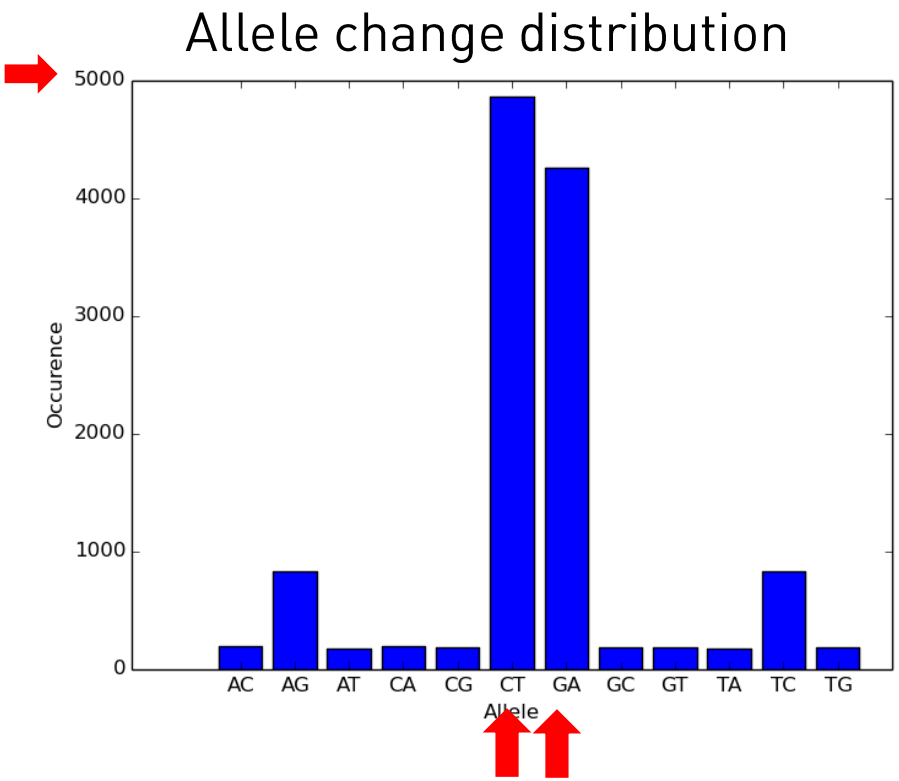
Damage correction followed by GATK recalibration



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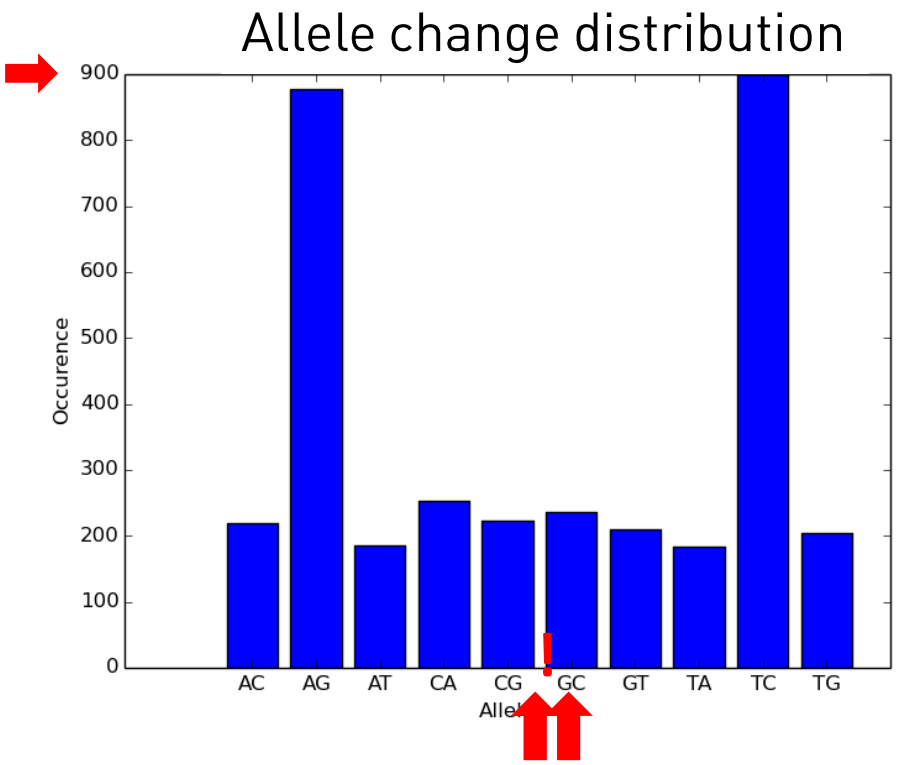
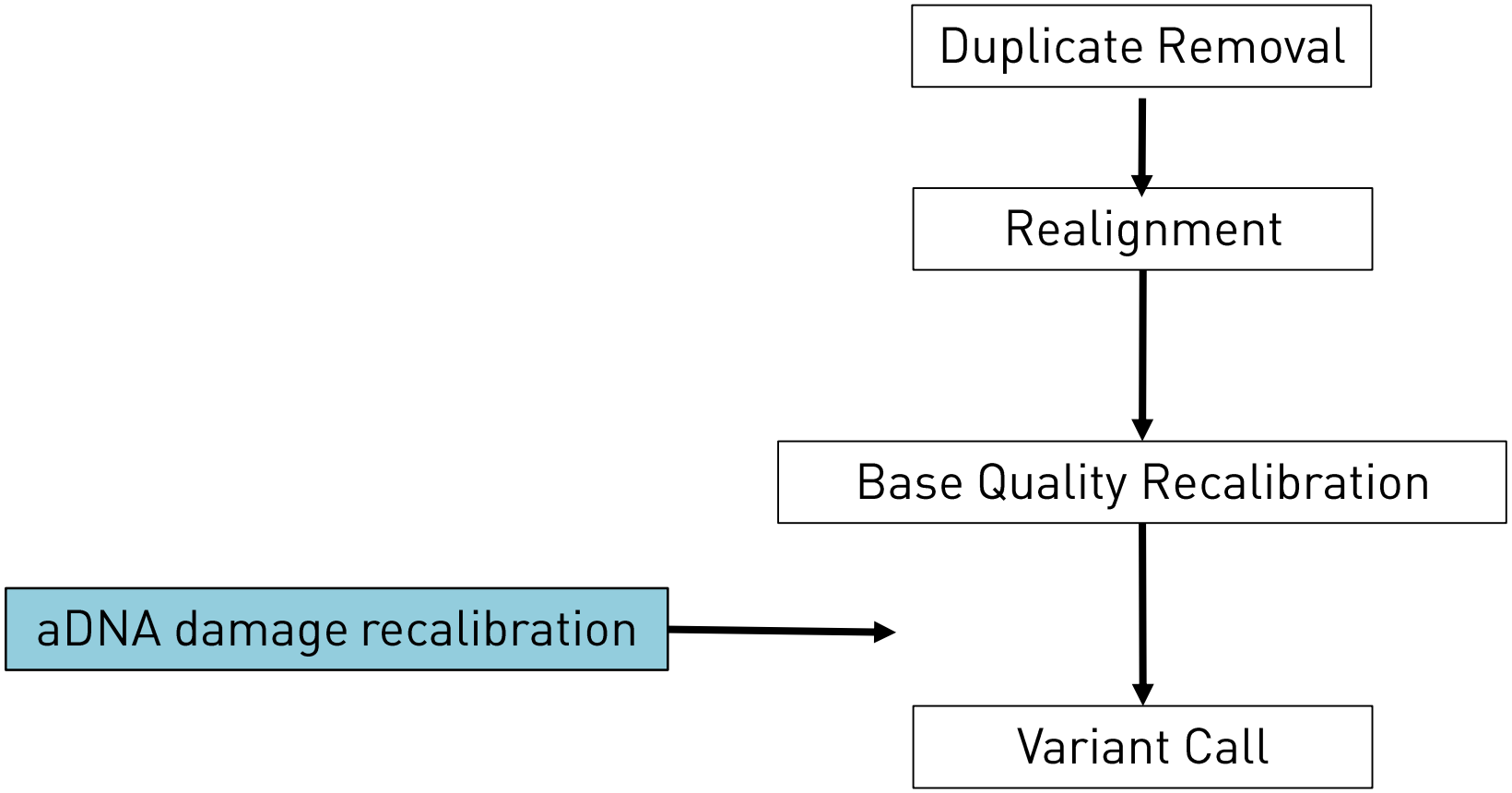


Corrected + recalibrated

Damage recalibration



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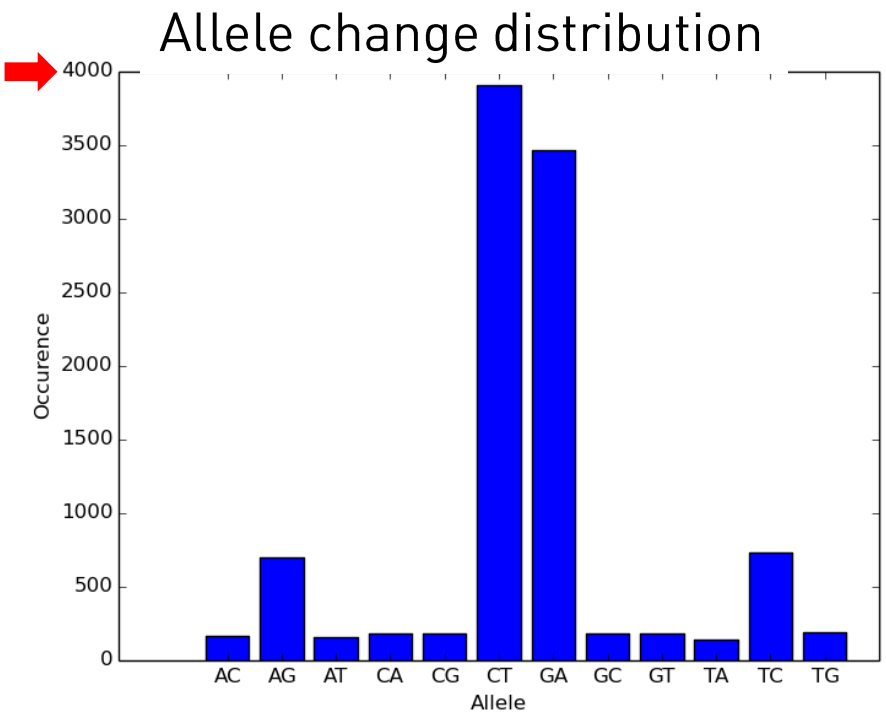
GATK recalibration



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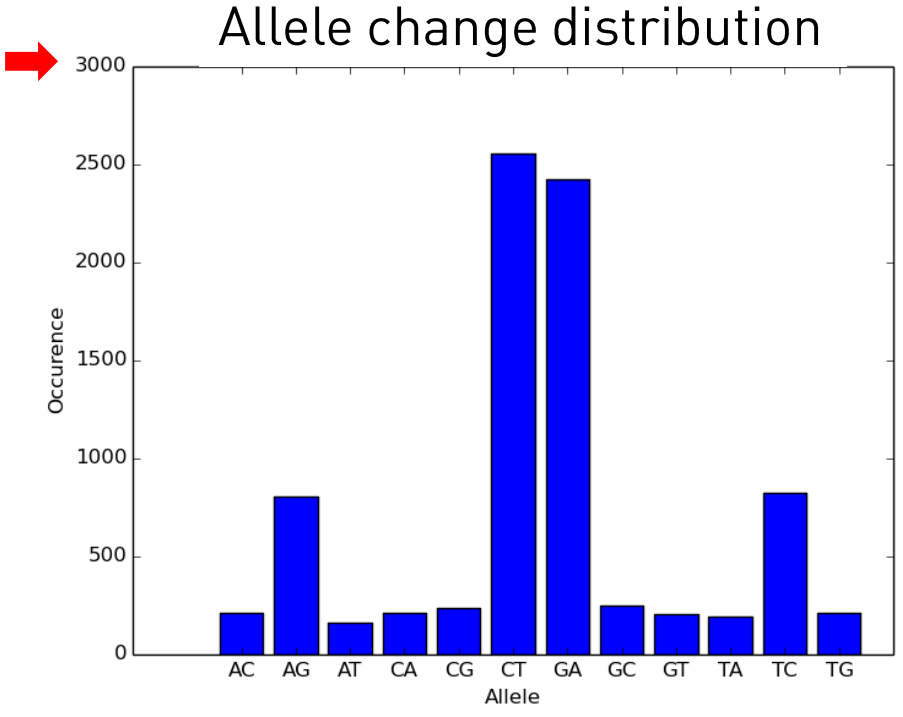

GATK recalibrated

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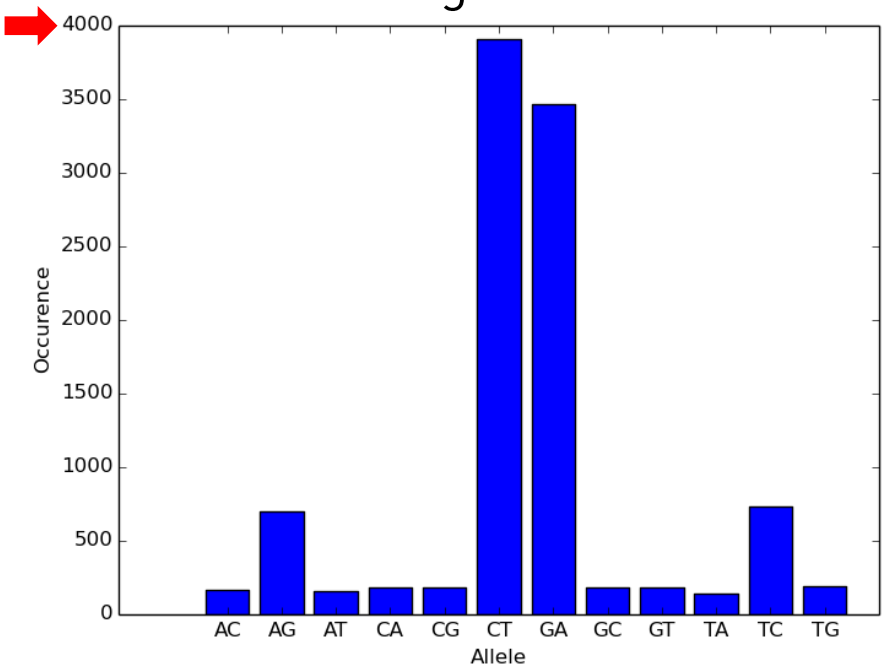
GATK recalibration followed by damage correction

Allele change distribution



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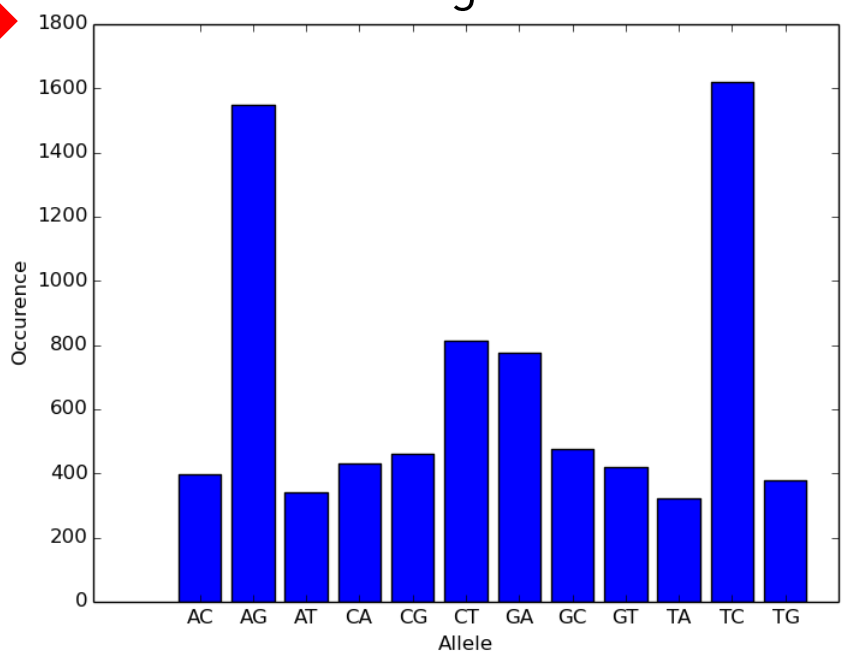
Allele change distribution



Damage and GATK recalibrated

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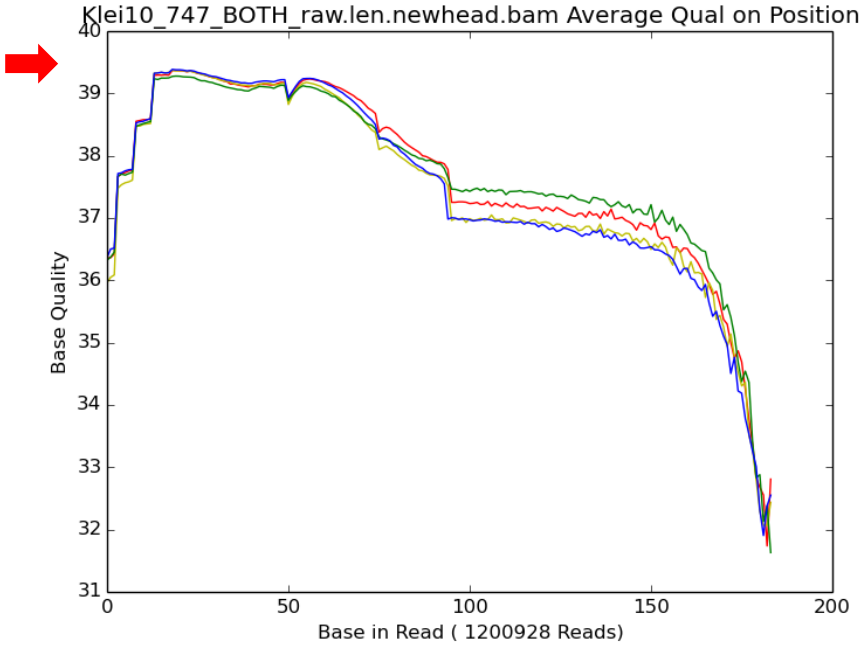
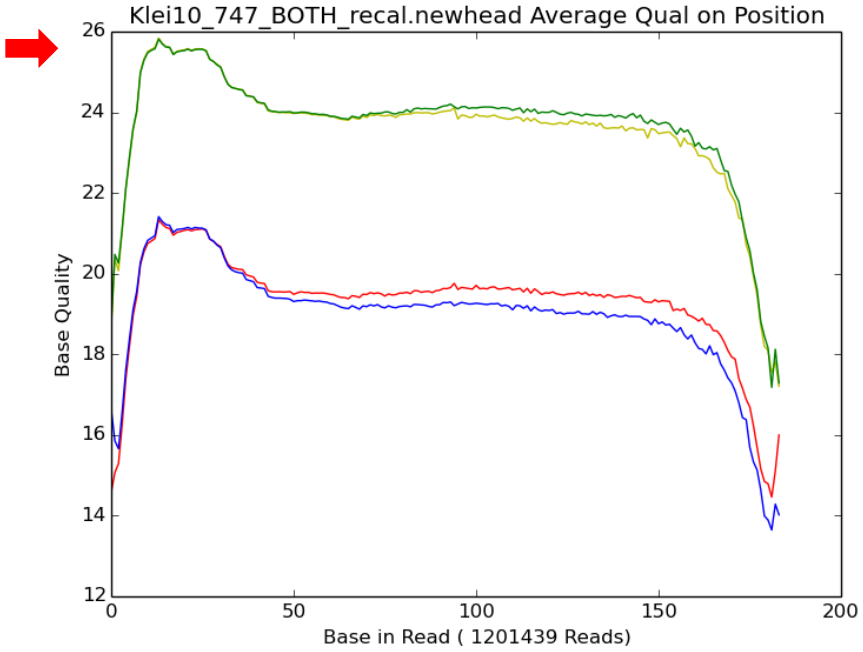
GATK recal followed by damage recalibration

Average Base quality/position/base

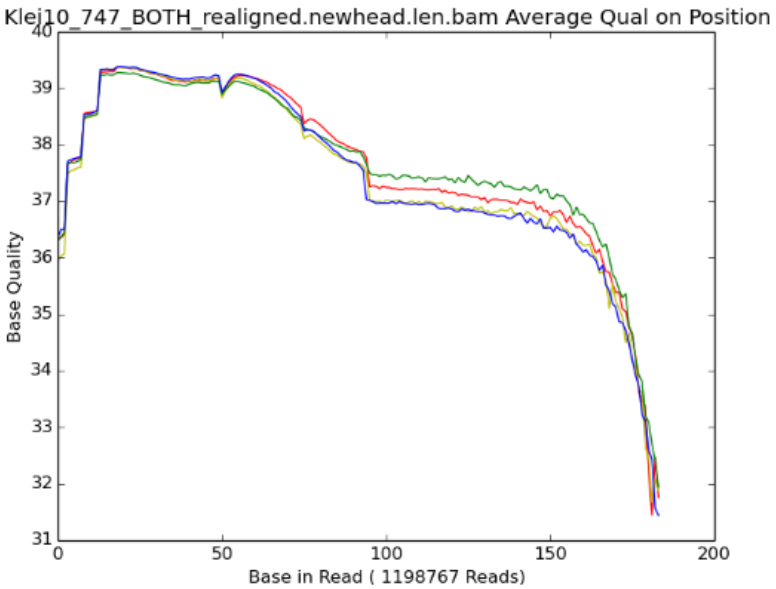


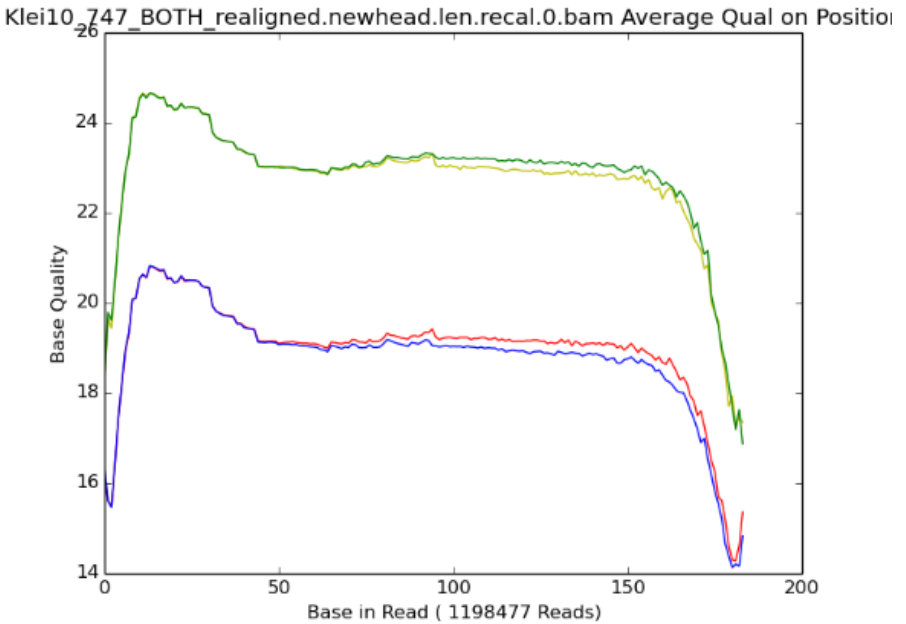


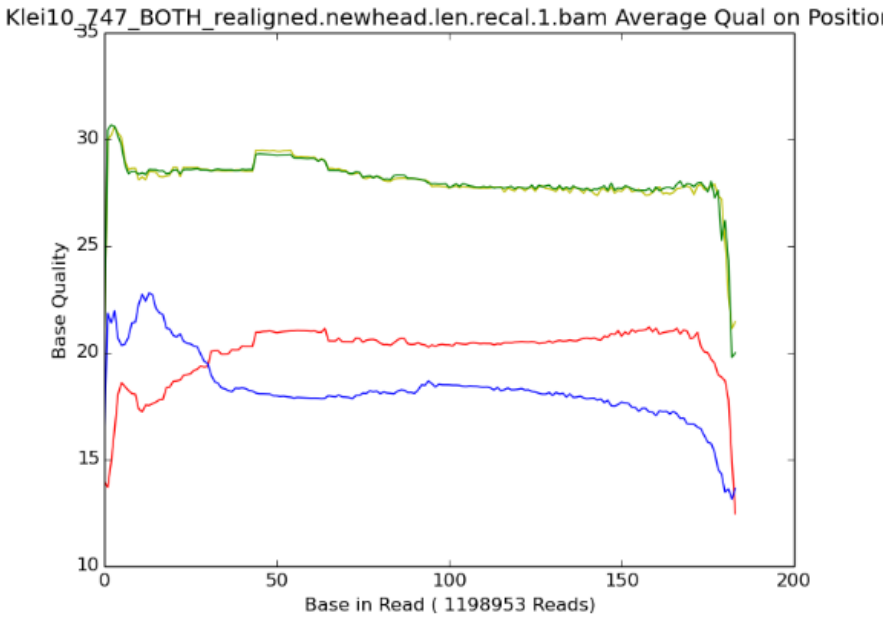
Base	Average	Min	Max
T (red)	37.63	31.74	39.37
STD	3.15	1.53	4.08
A (blue)	37.47	31.90	39.39
STD	3.23	1.58	4.21
C (yellow)	37.46	32.07	39.37
STD	3.28	1.46	4.49
G (green)	37.46	32.07	39.37
STD	3.28	1.46	4.49

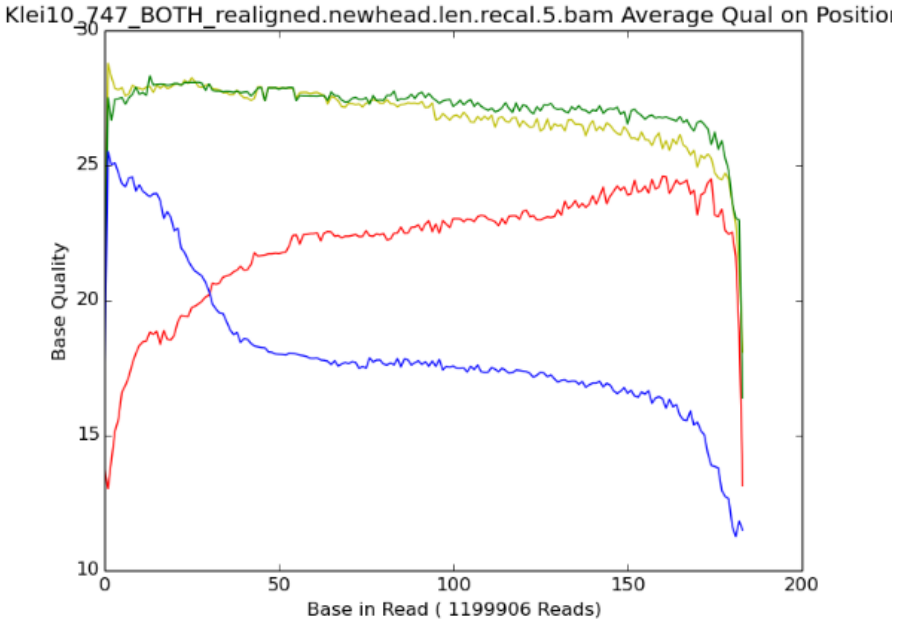
Base	Average	Min	Max
T (red)	19.29	14.46	21.34
STD	2.87	1.07	4.76
A (blue)	18.98	13.65	21.41
STD	3.27	1.99	4.14
C (yellow)	23.58	17.21	25.84
STD	2.82	1.46	4.05
G (green)	23.58	17.21	25.84
STD	2.82	1.46	4.05

GATK recalibration

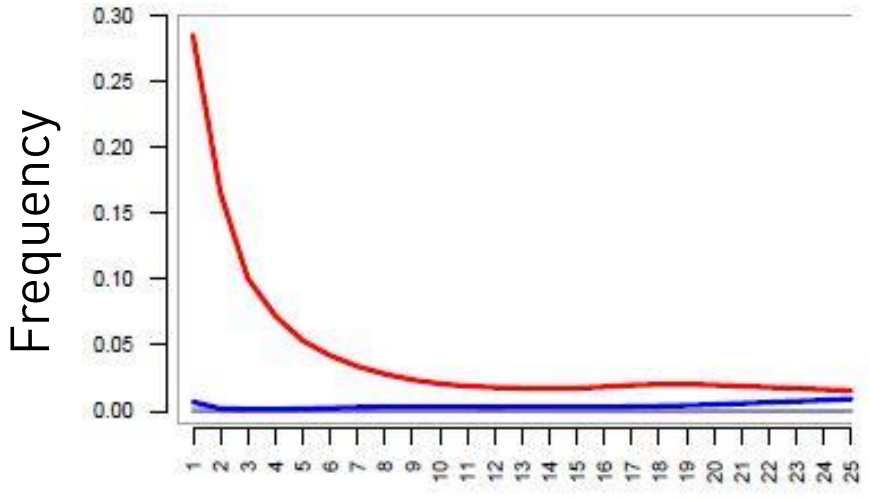




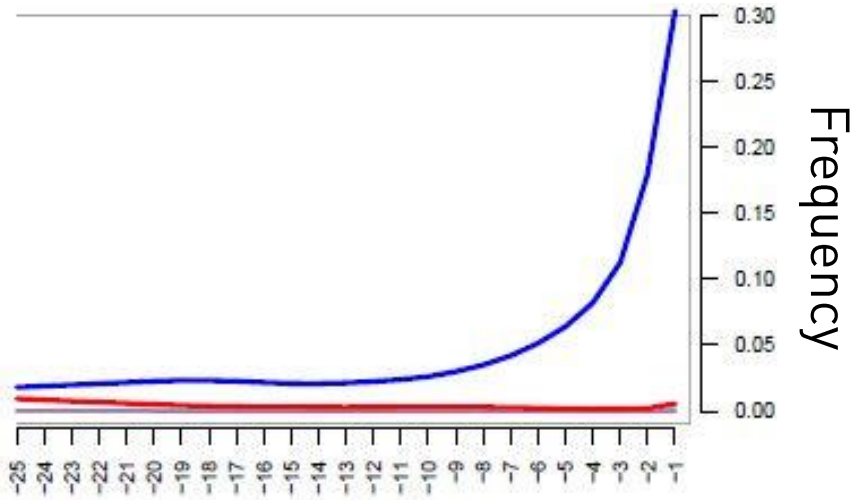




Postmortem damage patterns



Position in read relative to 5'



Position in read relative to 3'

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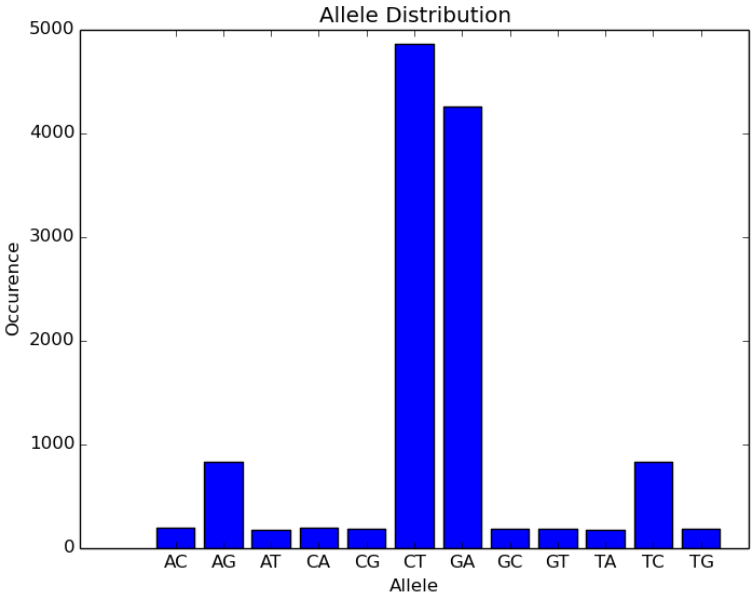
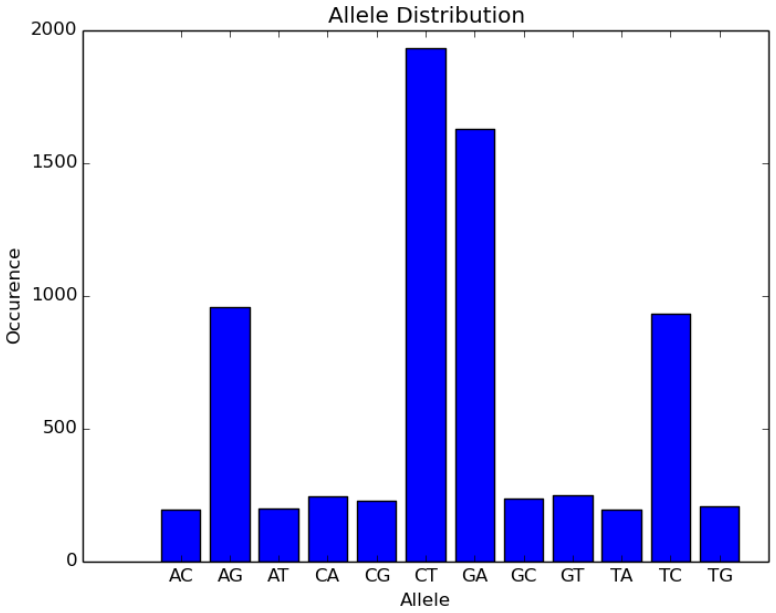
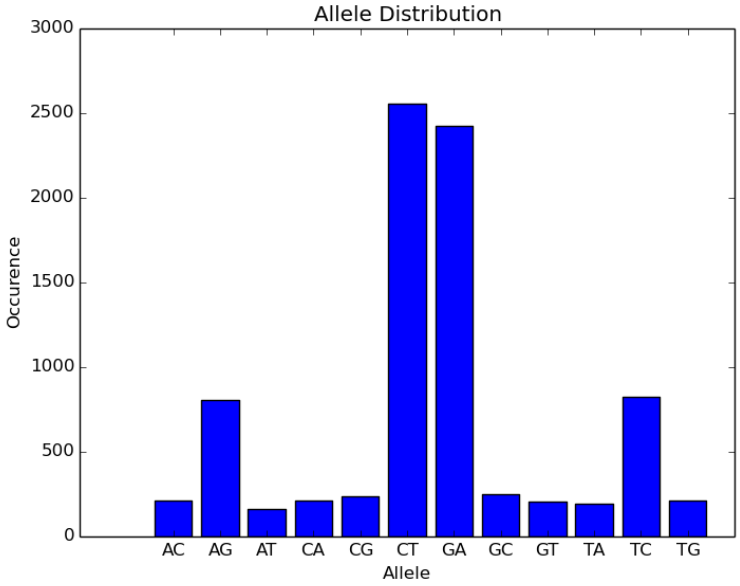
Raw data



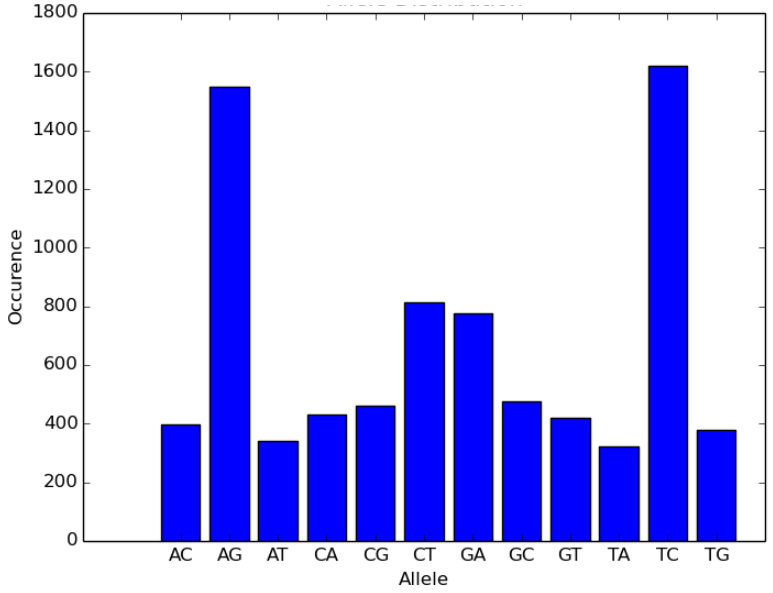
Damage recalibration



GATK recalibrated

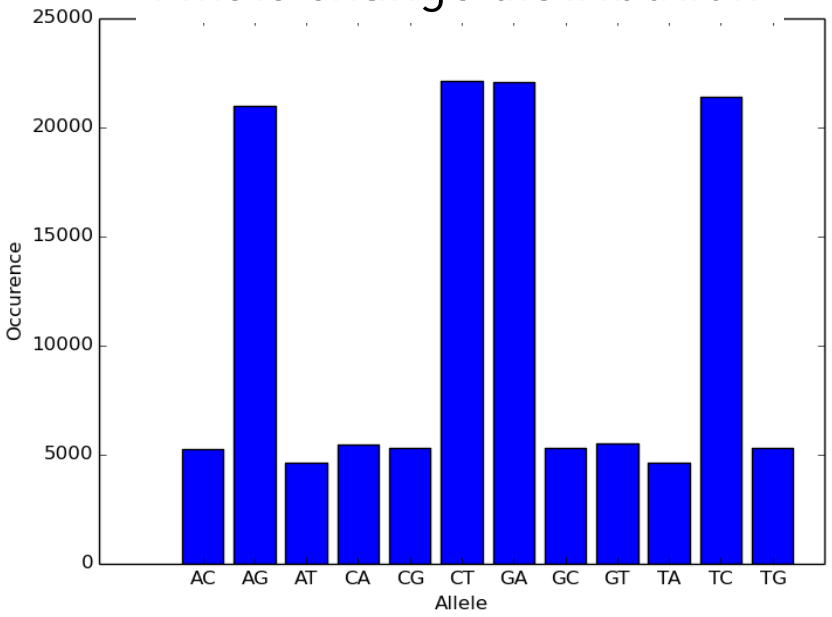


GATK recalibrated + damage recalibrated



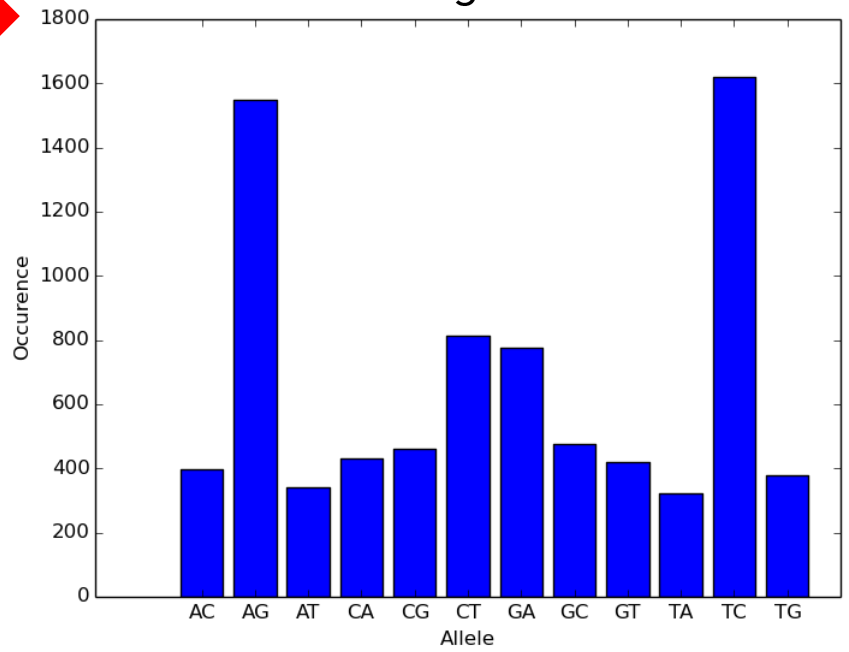
GATK recalibration followed by damage correction

Allele change distribution



Modern sample

Allele change distribution



Damage and GATK recalibrated

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Current work

- Developing a maximum-likelihood based based SNP caller that incorporates damage correction and base recalibration into the variant calling framework
- Frees aDNA-based variant calling and genotyping from excessive dependence of modern reference
- Addresses the problem of over-training and over-correcting by running damage correction and recalibration simultaneously

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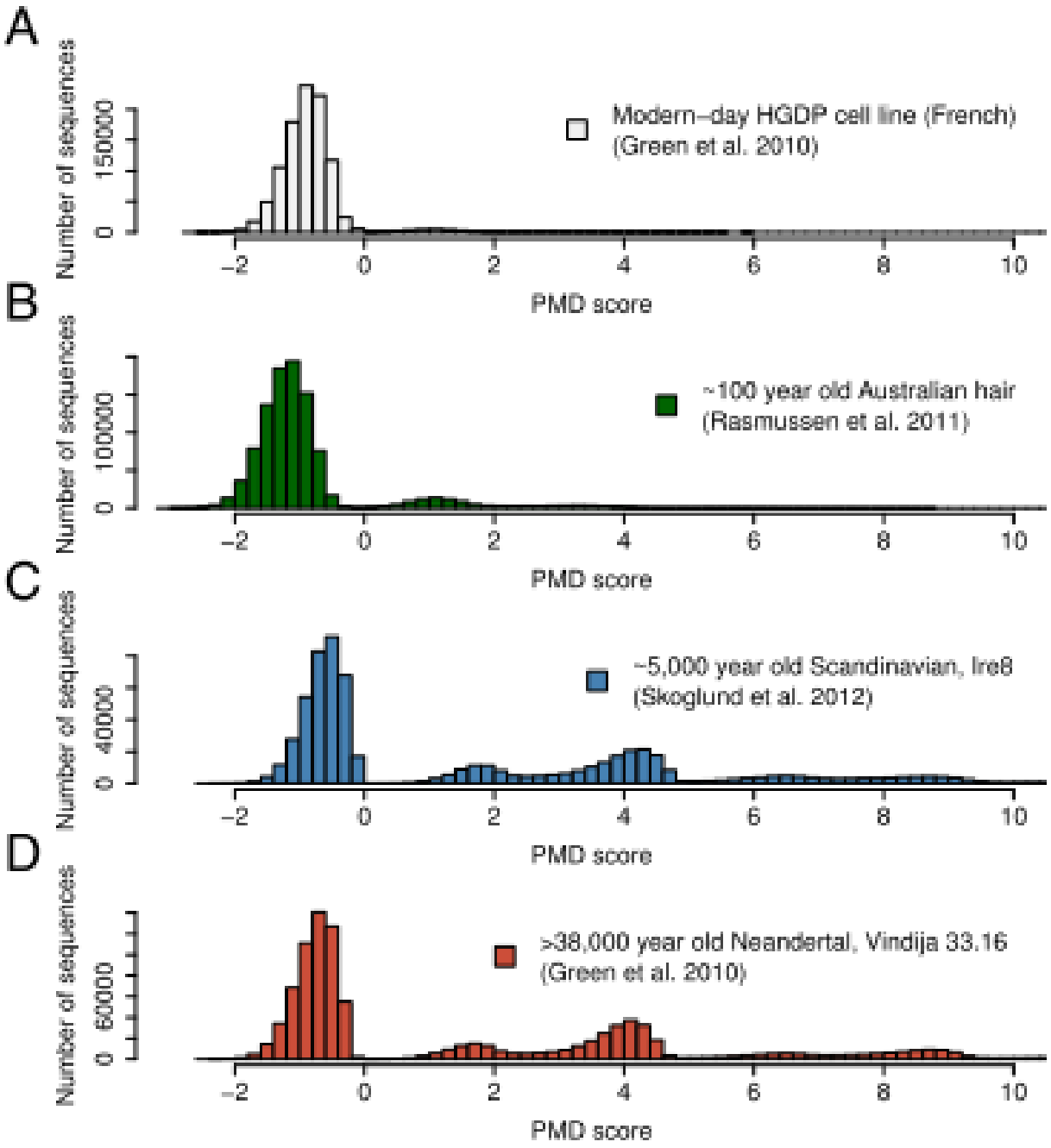
STONY BROOK UNIVERSITY

GeneRED

UNIVERSITAS FRIBURGENSIS



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