PREDICTION OF PATHOGENIC SNV

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6 CFU

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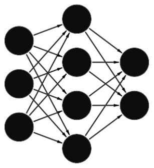
Lecture Notes
Year 2017/2018



IT Master Degree
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Indice

Parte I

Dataset

1

Data points

First we begin looking at the dataset, the distributions of the given metrics and the statistical analysis of these data points.

1.1 Retrieving the dataset

The dataset can be downloaded from https://homes.di.unimi.it/valentini/ProgettoBioinformatica1718/data/.

1.2 Data points

In the dataset there are 981389 data points, each one comprised of 26 metrics. The first 356 are pathogenic and all the others are negative.

2

Metrics

2.1 CpGobsExp

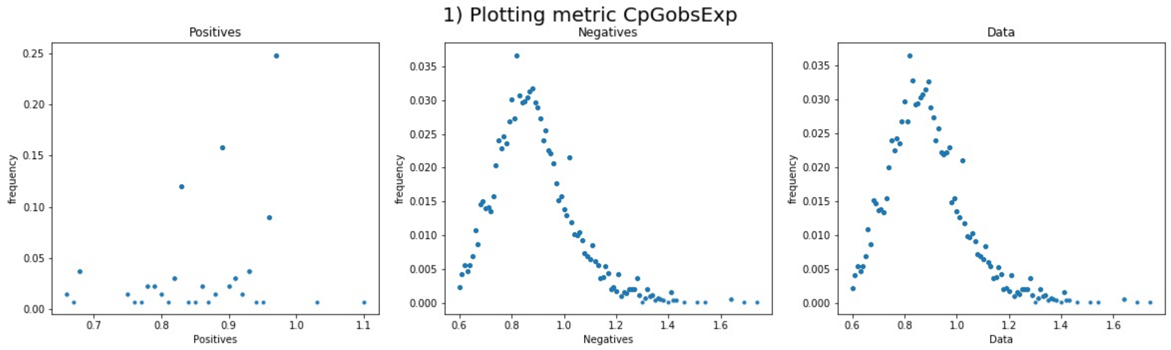

Figura 2.1: Sampling distribution of metric CpGobsExp

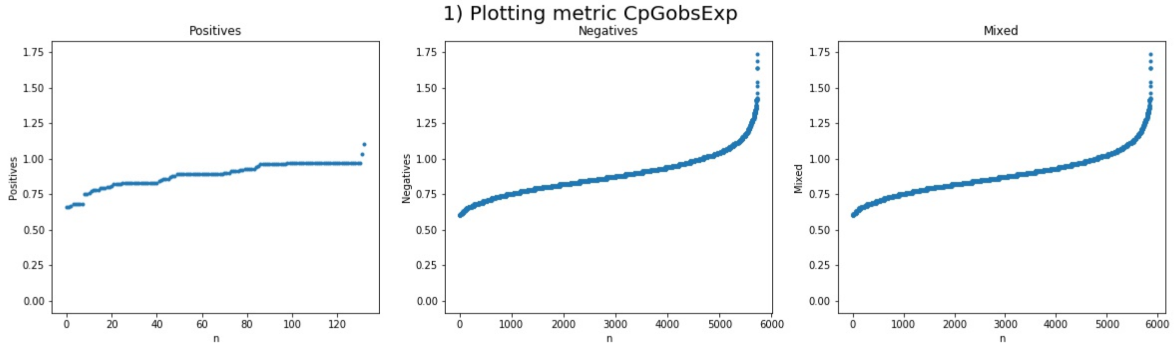

Figura 2.2: Values of metric CpGobsExp

2.2 CpGperCpG

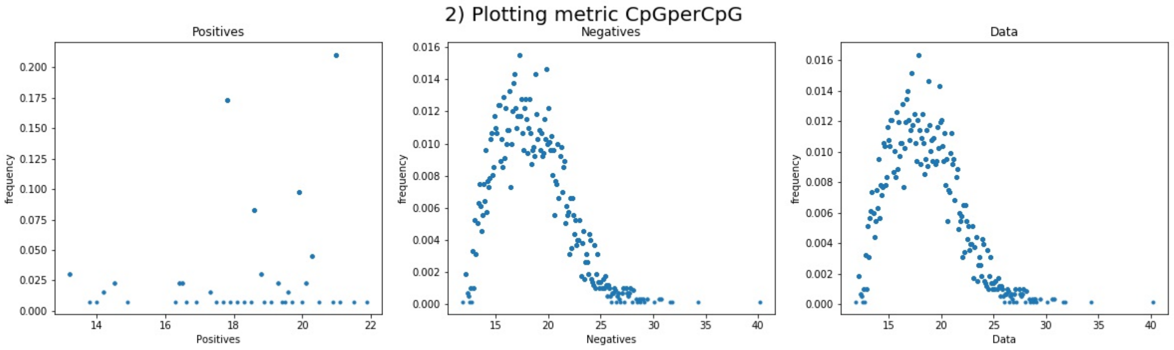

Figura 2.3: Sampling distribution of metric CpGperCpG

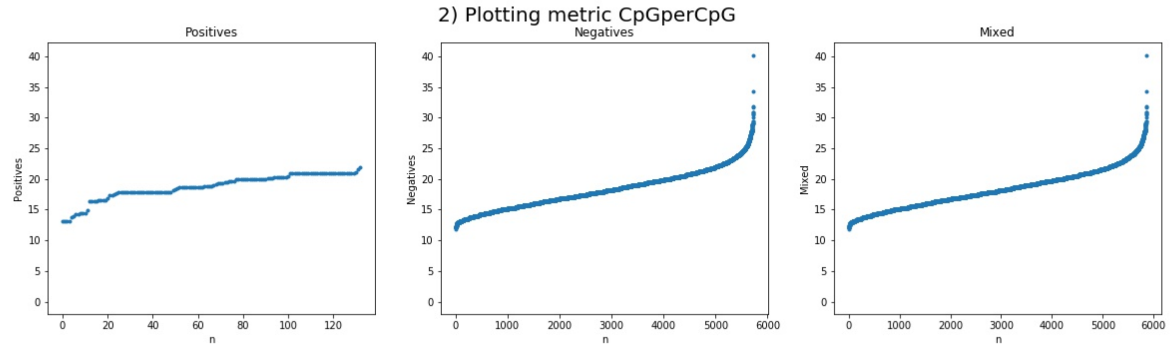

Figura 2.4: Values of metric CpGperCpG

2.3 CpGperGC

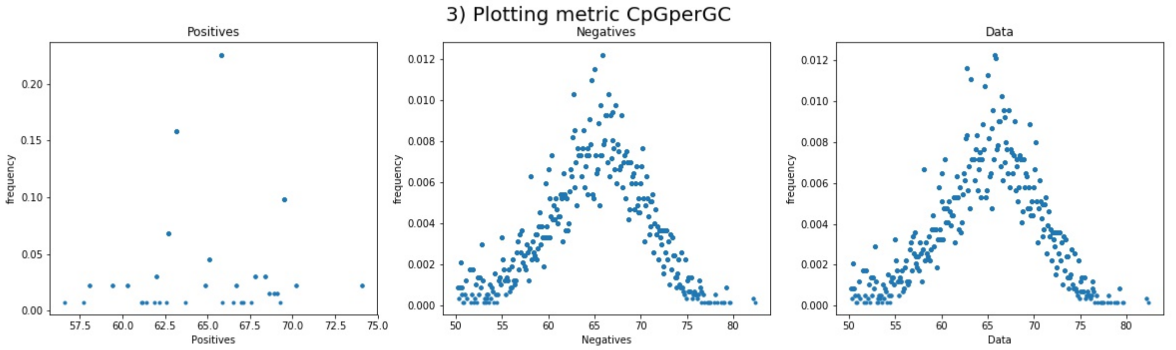

Figura 2.5: Sampling distribution of metric CpGperGC

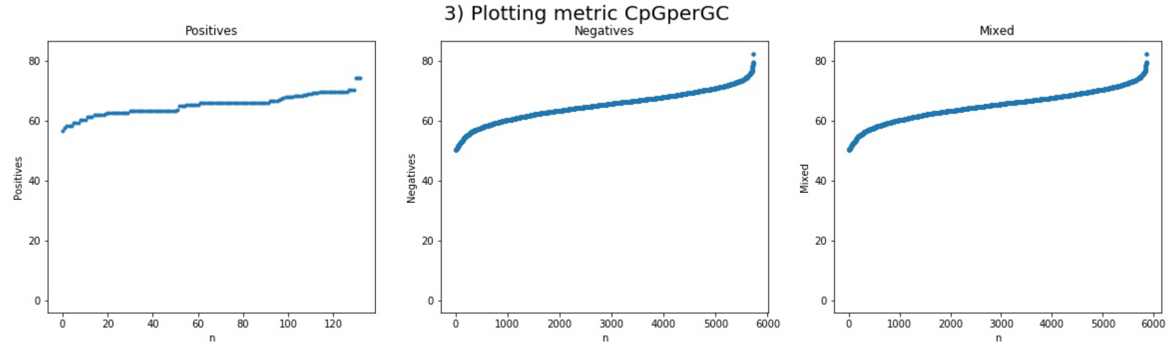

Figura 2.6: Values of metric CpGperGC

2.4 DGVCount

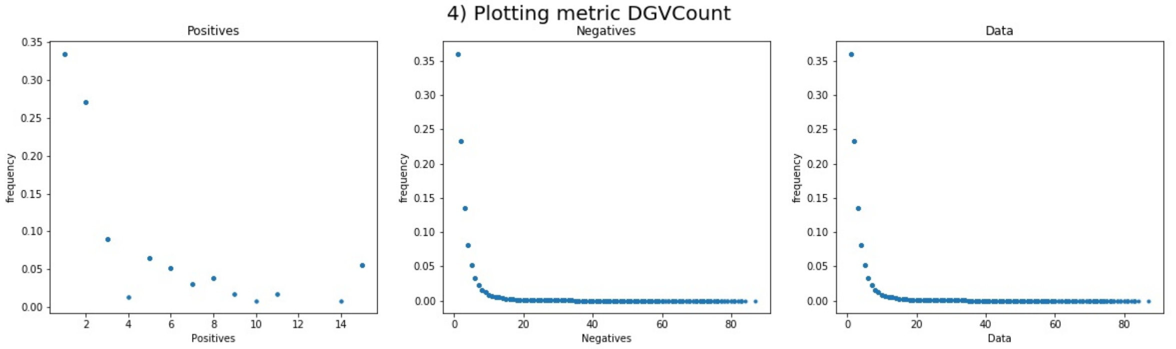

Figura 2.7: Sampling distribution of metric DGVCount

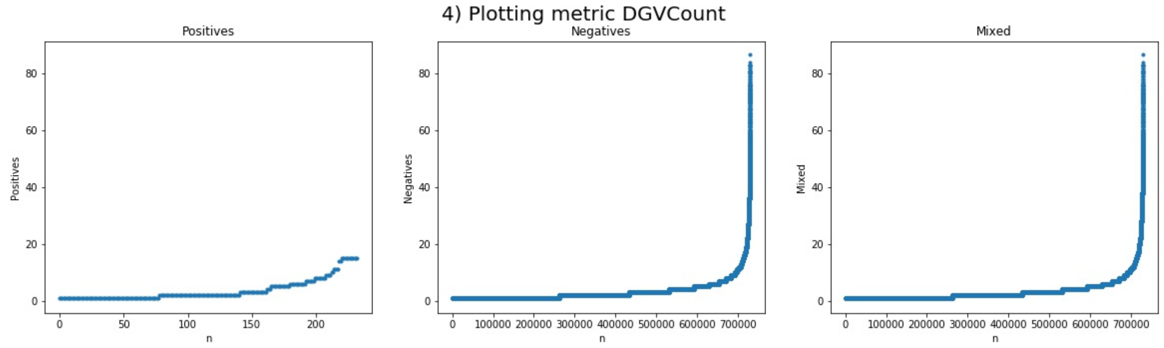

Figura 2.8: Values of metric DGVCount

2.5 DnaseClusteredHyp

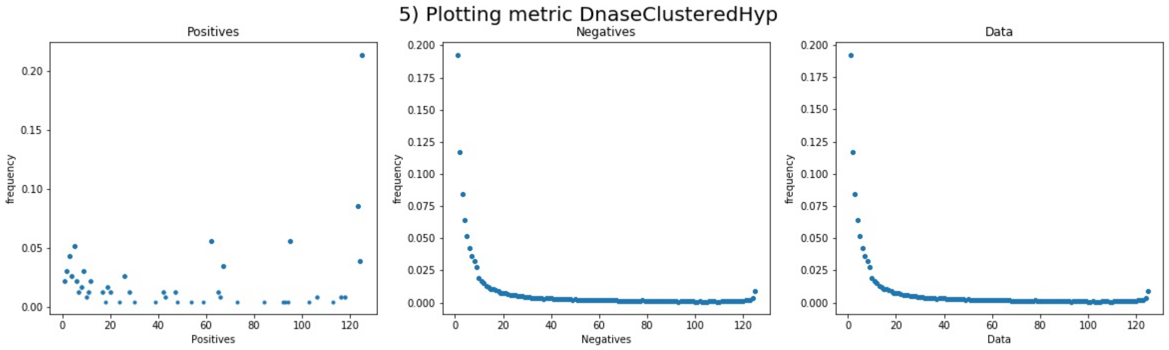

Figura 2.9: Sampling distribution of metric DnaseClusteredHyp

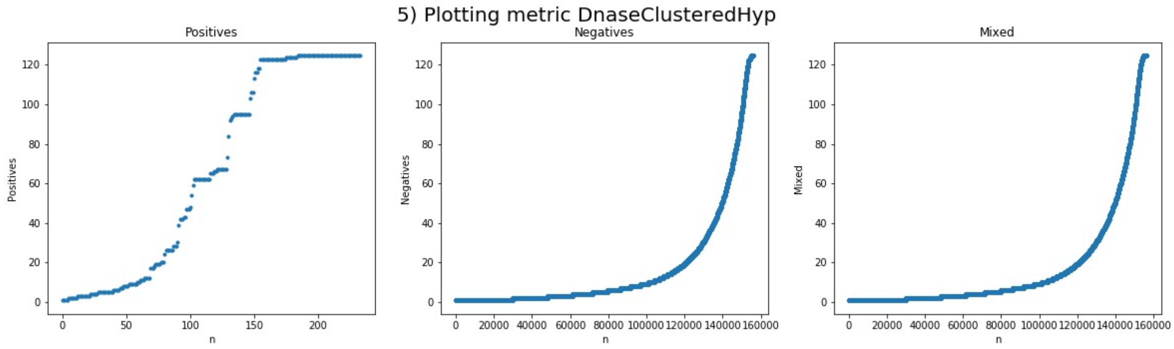

Figura 2.10: Values of metric DnaseClusteredHyp

2.6 DnaseClusteredScore

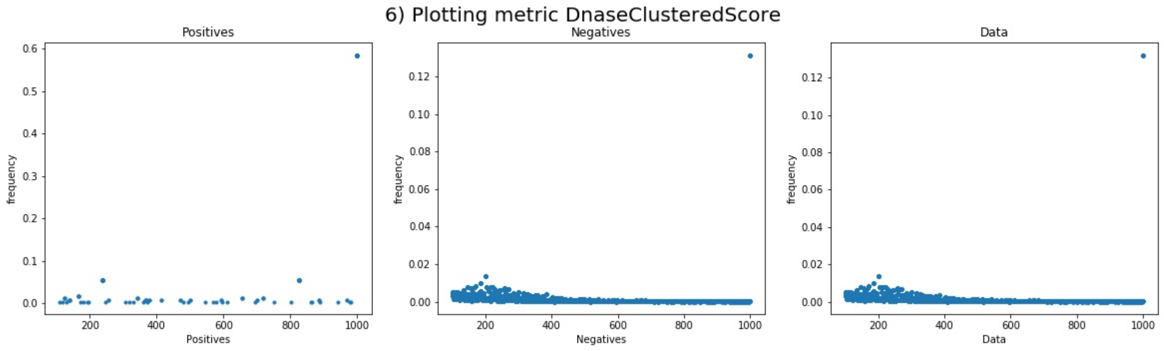

Figura 2.11: Sampling distribution of metric DnaseClusteredScore

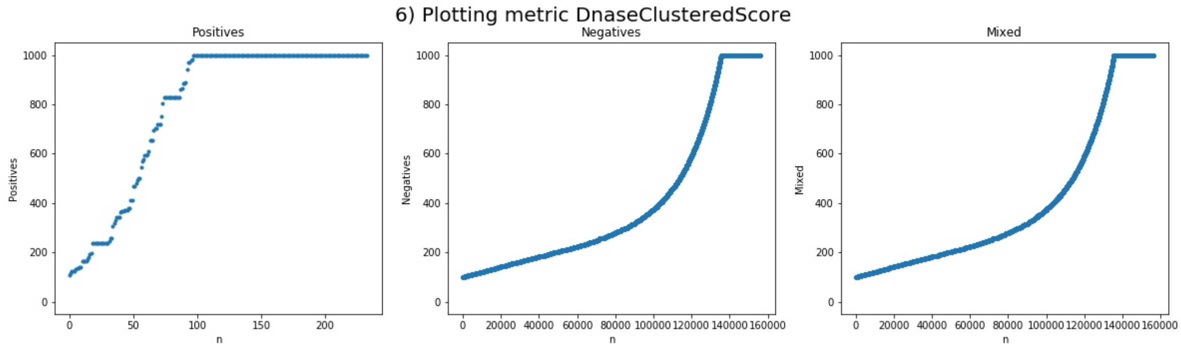

Figura 2.12: Values of metric DnaseClusteredScore

2.7 EncH3K27Ac

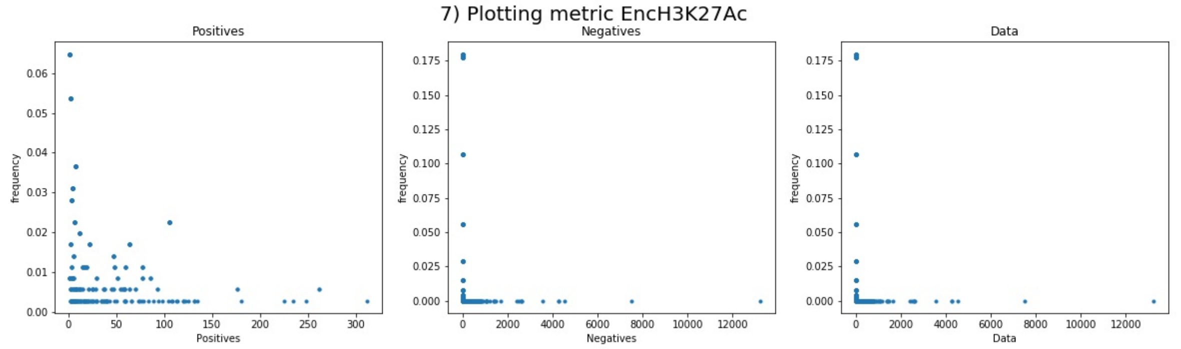

Figura 2.13: Sampling distribution of metric EncH3K27Ac

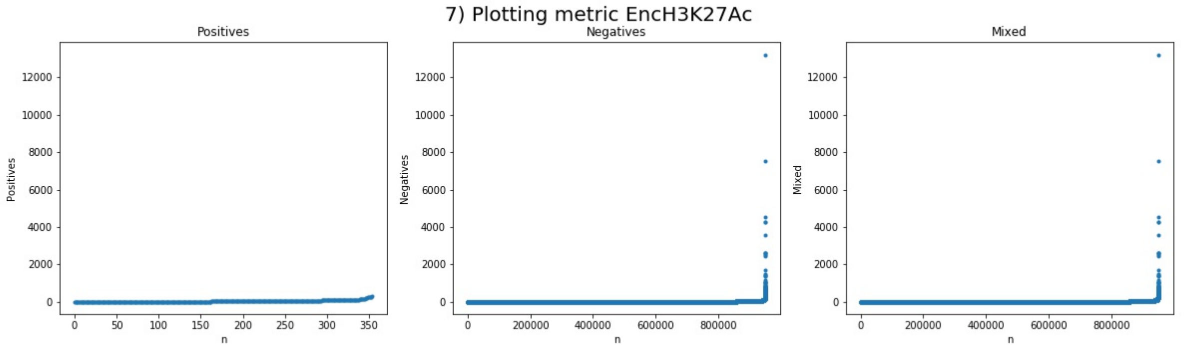

Figura 2.14: Values of metric EncH3K27Ac

2.8 EncH3K4Me1

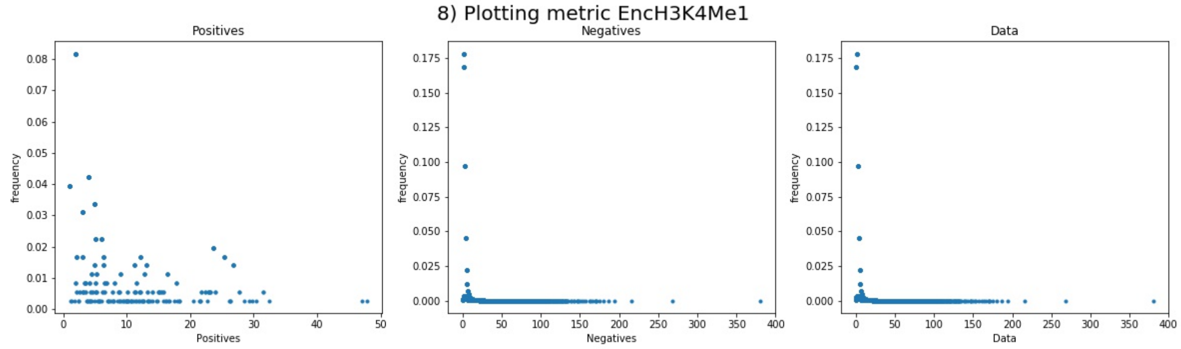

Figura 2.15: Sampling distribution of metric EncH3K4Me1

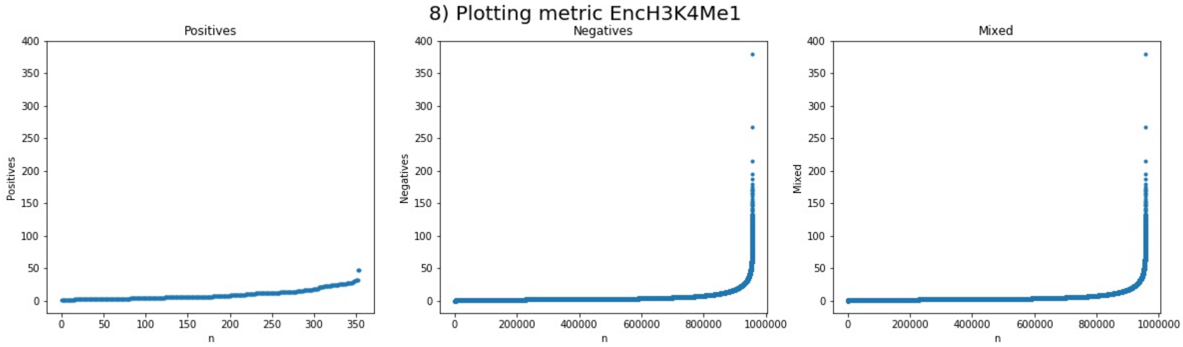

Figura 2.16: Values of metric EncH3K4Me1

2.9 EncH3K4Me3

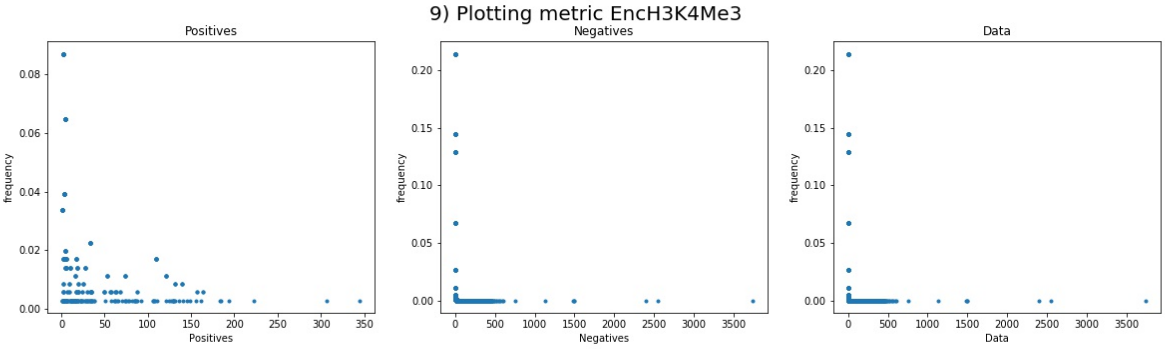

Figura 2.17: Sampling distribution of metric EncH3K4Me3

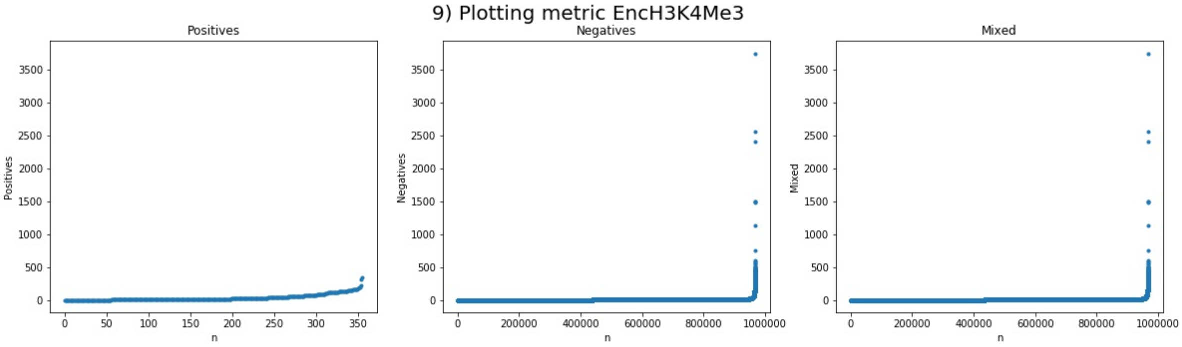

Figura 2.18: Values of metric EncH3K4Me3

2.10 GCContent

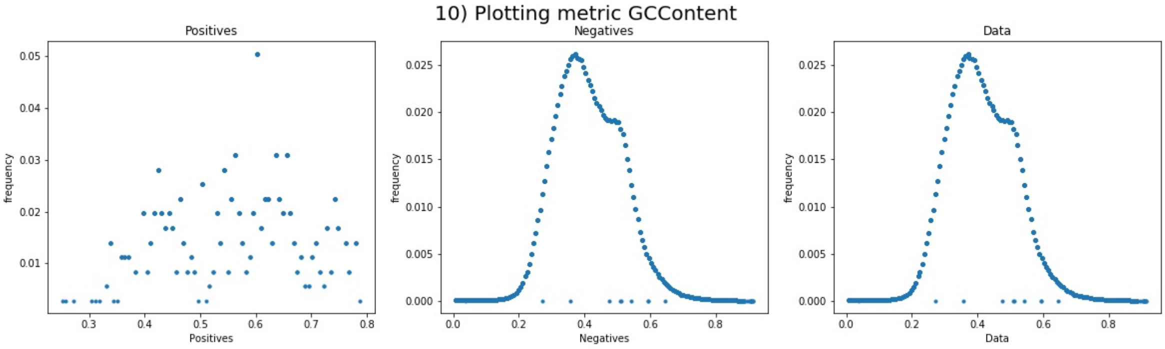

Figura 2.19: Sampling distribution of metric GCContent

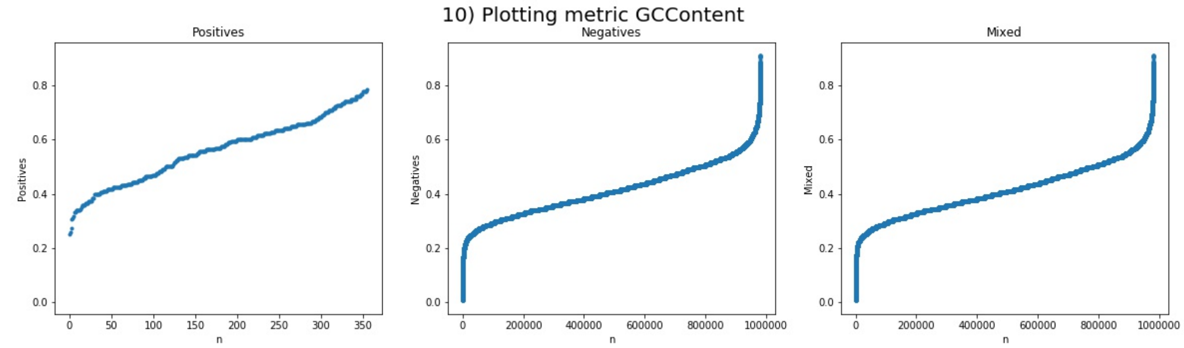

Figura 2.20: Values of metric GCContent

2.11 GerpRS

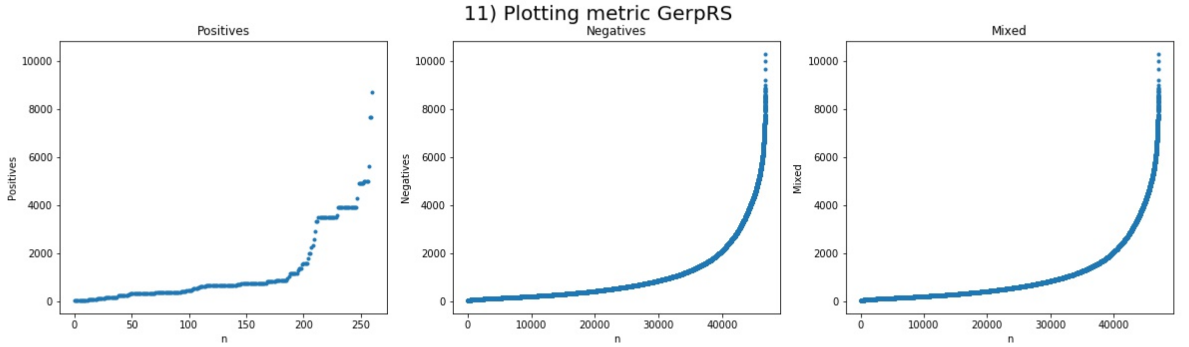

Figura 2.21: Values of metric GerpRS

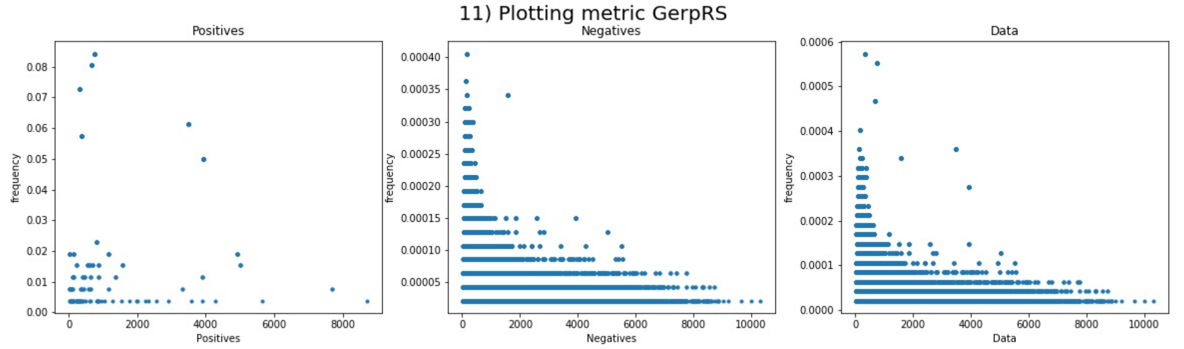

Figura 2.22: Sampling distribution of metric GerpRS

2.12 GerpRSpv

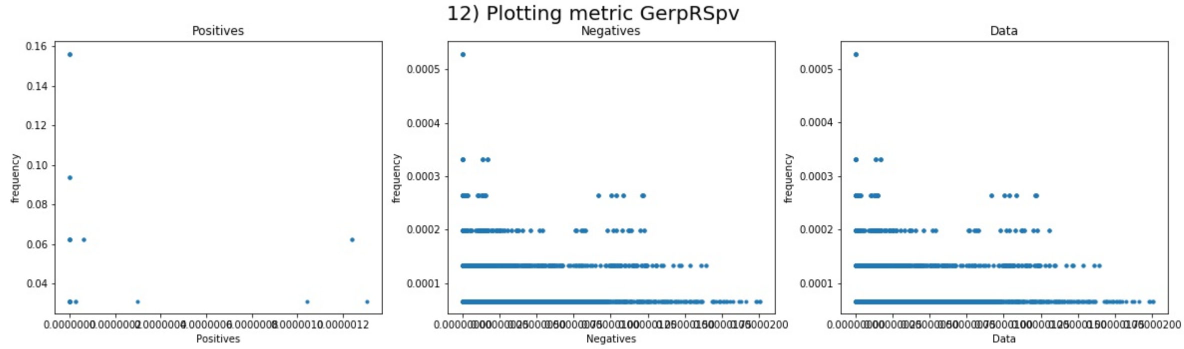

Figura 2.23: Sampling distribution of metric GerpRSpv

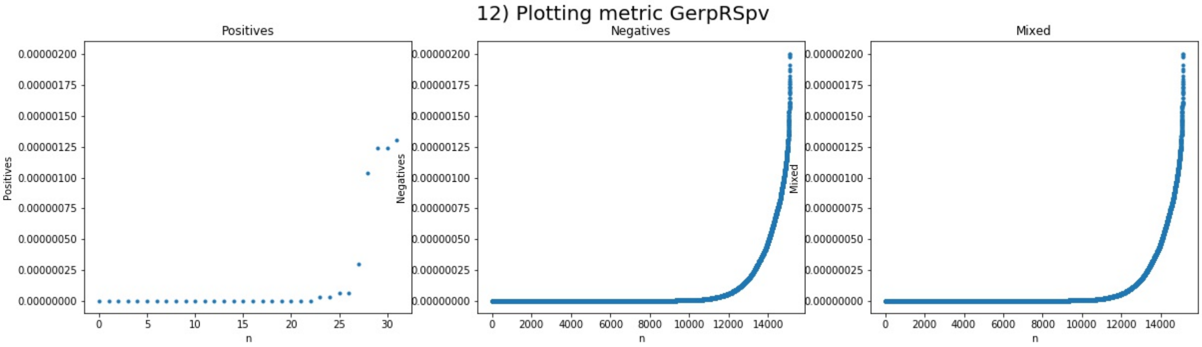

Figura 2.24: Values of metric GerpRSpv

2.13 ISCApath

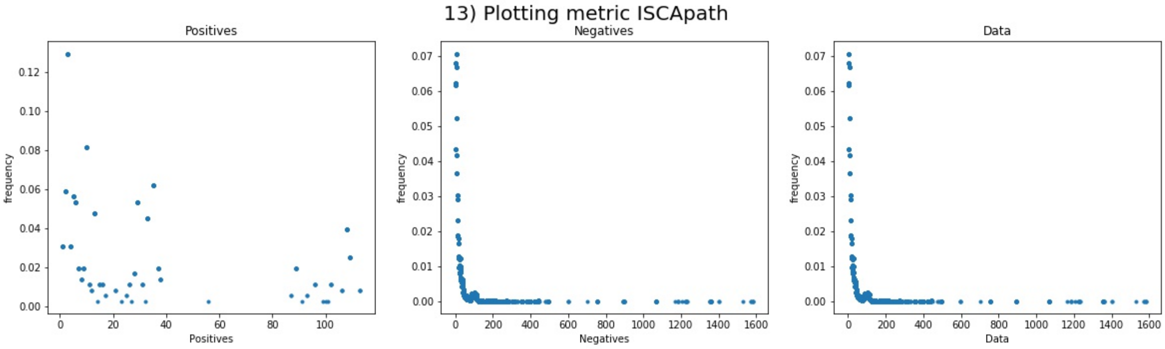

Figura 2.25: Sampling distribution of metric ISCApath

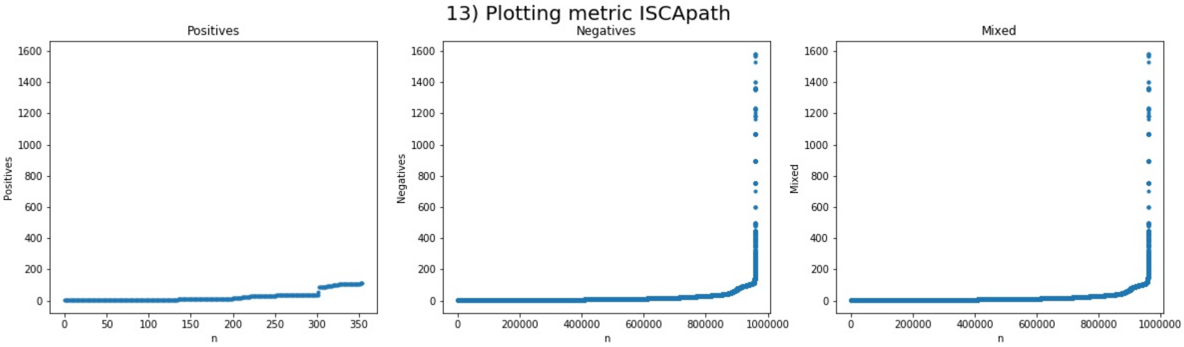

Figura 2.26: Values of metric ISCApath

2.14 commonVar

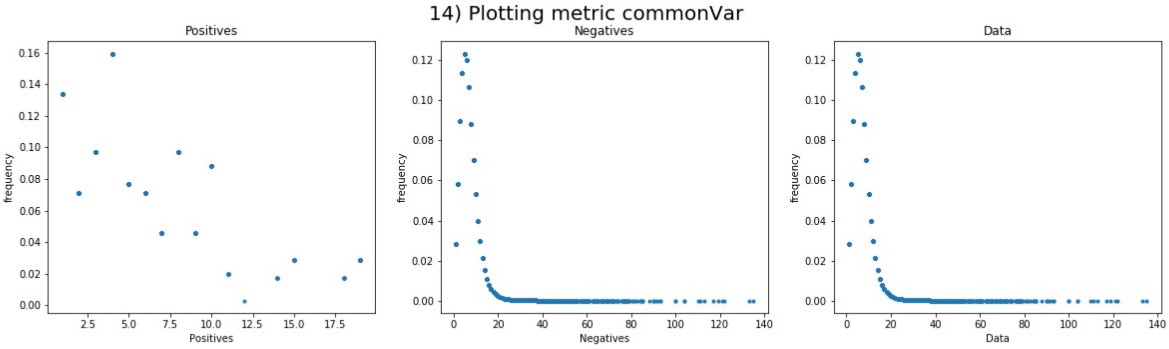

Figura 2.27: Sampling distribution of metric commonVar

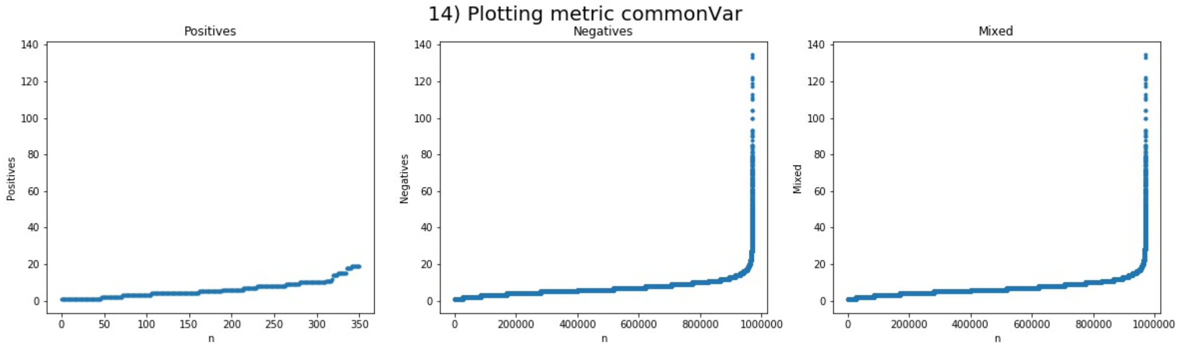

Figura 2.28: Values of metric commonVar

2.15 dbVARCount

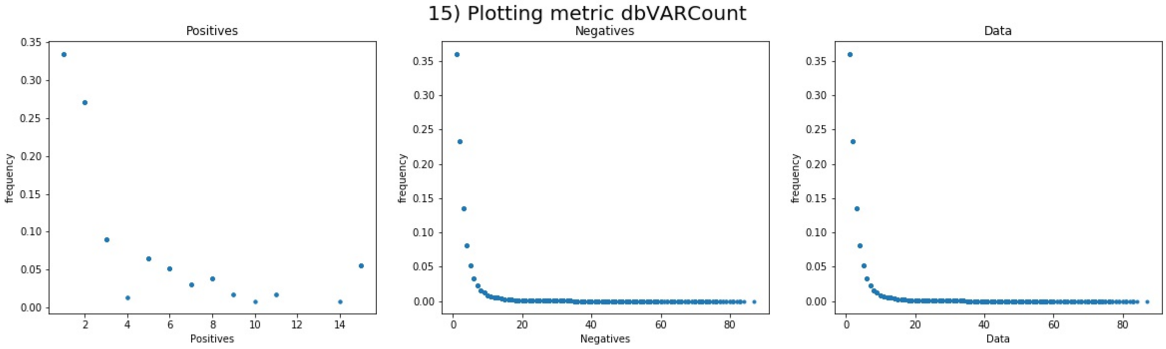

Figura 2.29: Sampling distribution of metric dbVARCount

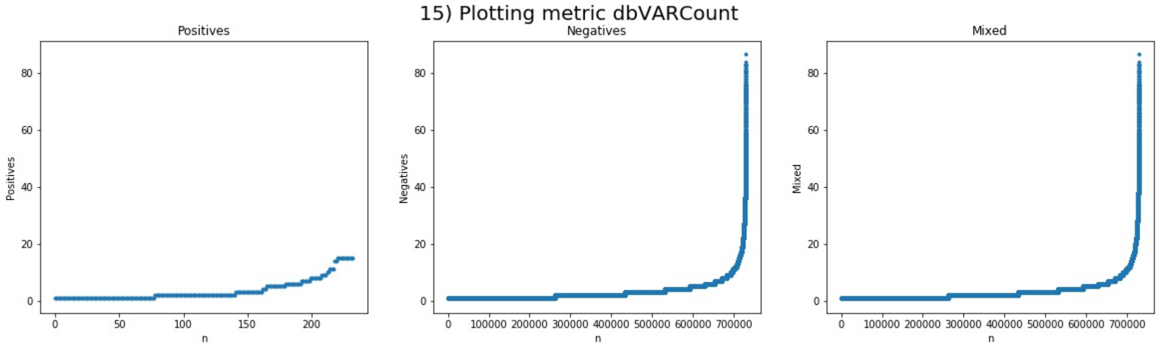

Figura 2.30: Values of metric dbVARCount

2.16 fantom5Perm

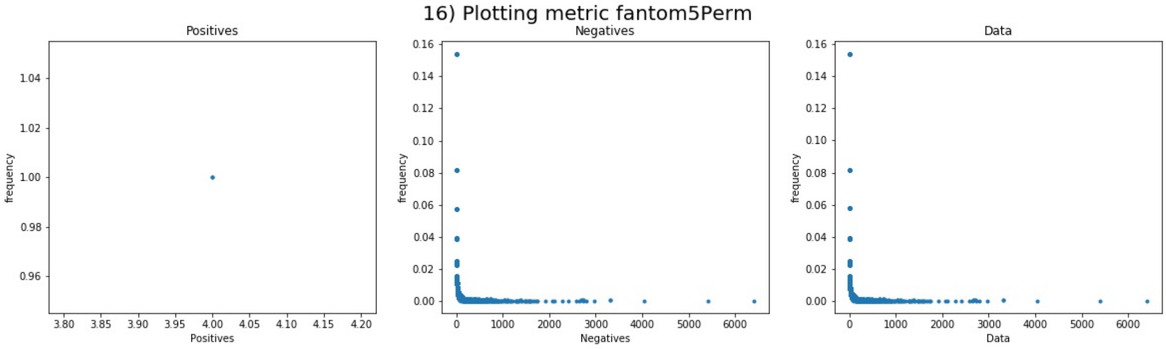

Figura 2.31: Sampling distribution of metric fantom5Perm

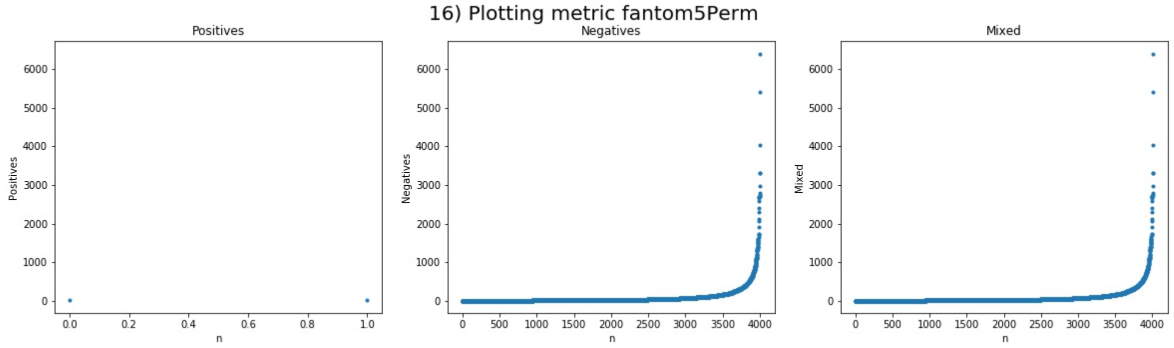

Figura 2.32: Values of metric fantom5Perm

2.17 fantom5Robust

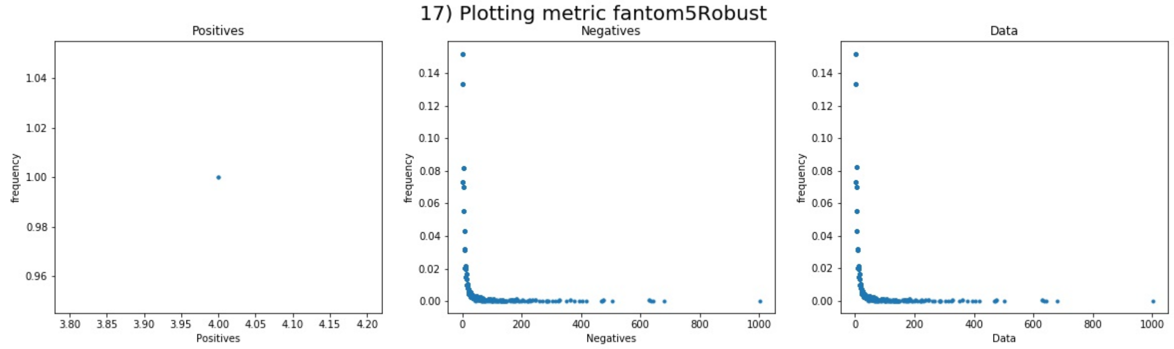

Figura 2.33: Sampling distribution of metric fantom5Robust

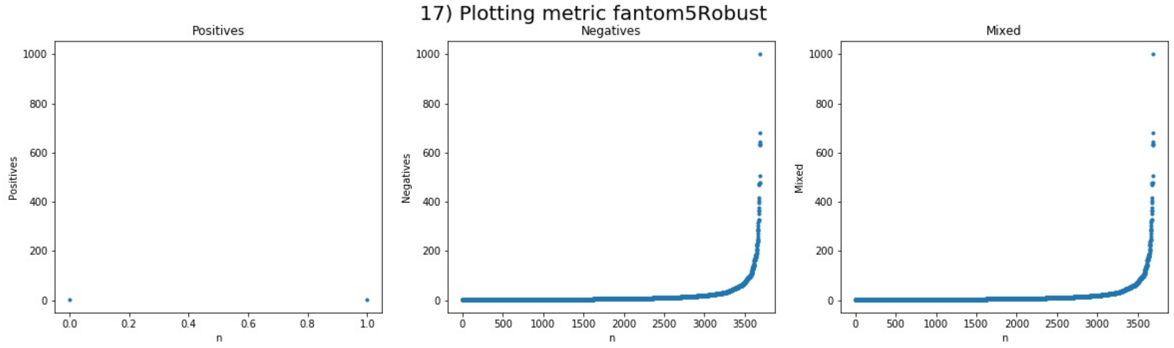

Figura 2.34: Values of metric fantom5Robust

2.18 fracRareCommon

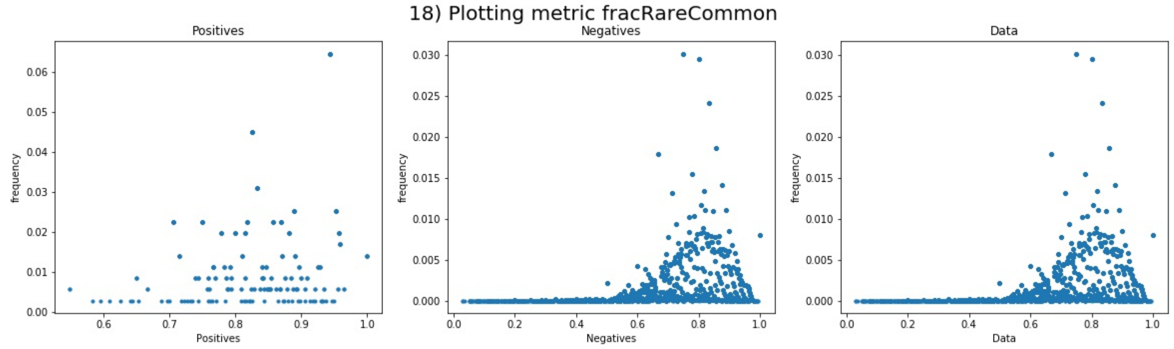

Figura 2.35: Sampling distribution of metric fracRareCommon

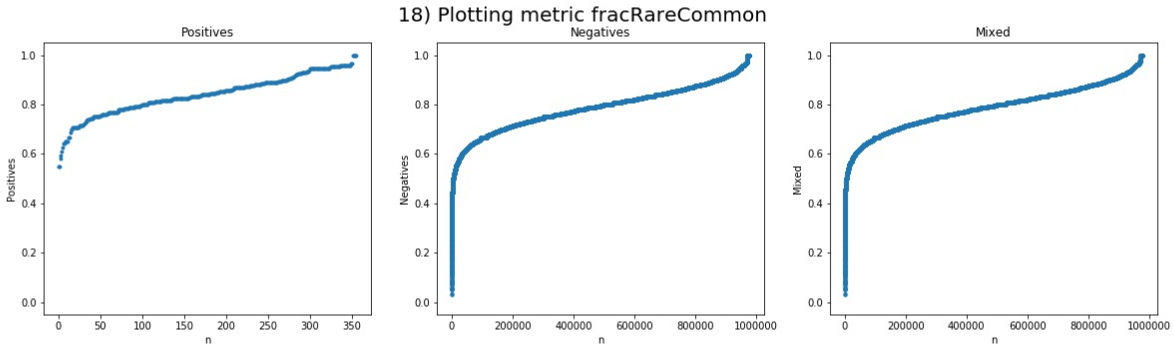

Figura 2.36: Values of metric fracRareCommon

2.19 mamPhastCons46way

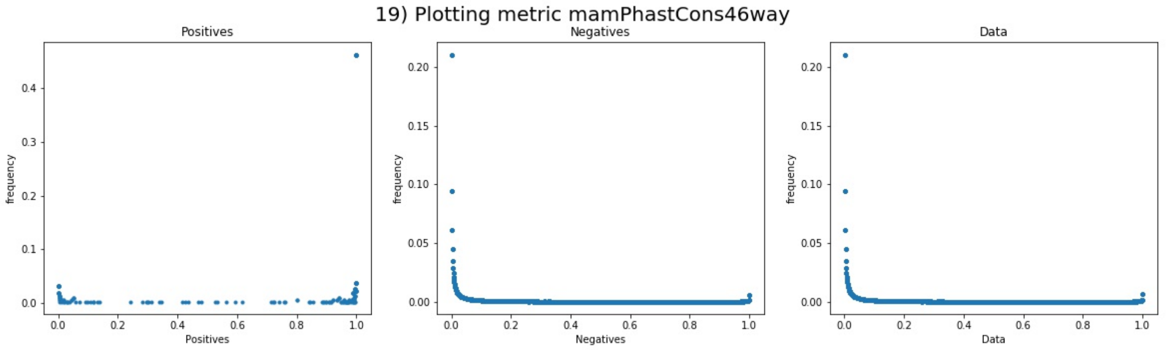

Figura 2.37: Sampling distribution of metric mamPhastCons46way

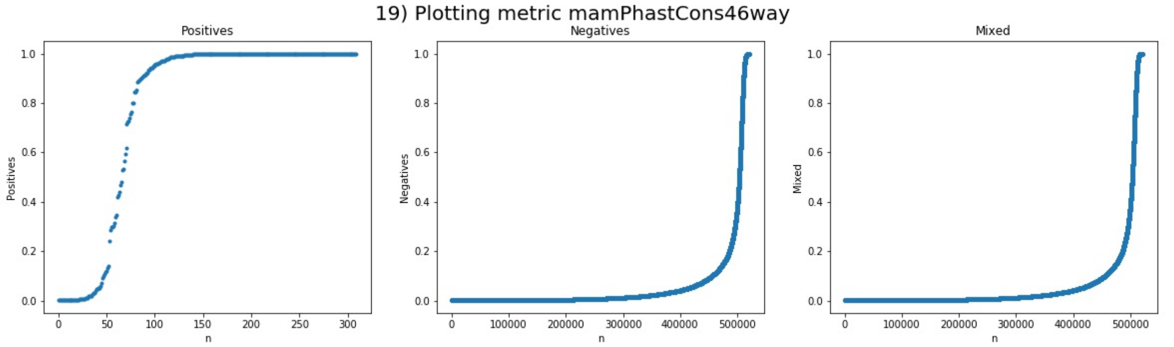

Figura 2.38: Values of metric mamPhastCons46way

2.20 mamPhyloP46way

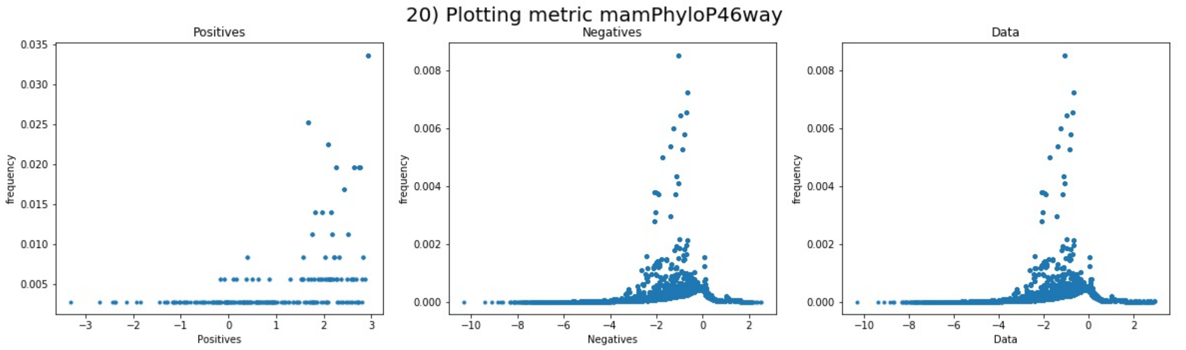

Figura 2.39: Sampling distribution of metric mamPhyloP46way

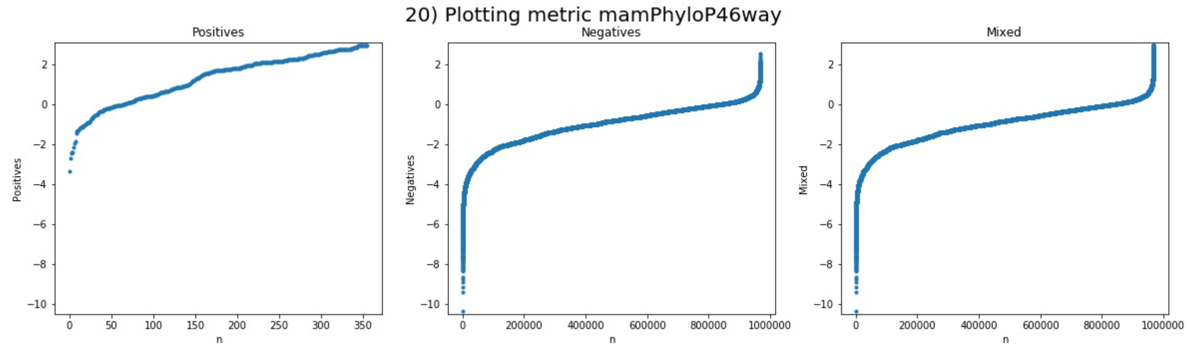

Figura 2.40: Values of metric mamPhyloP46way

2.21 numTFBSConserved

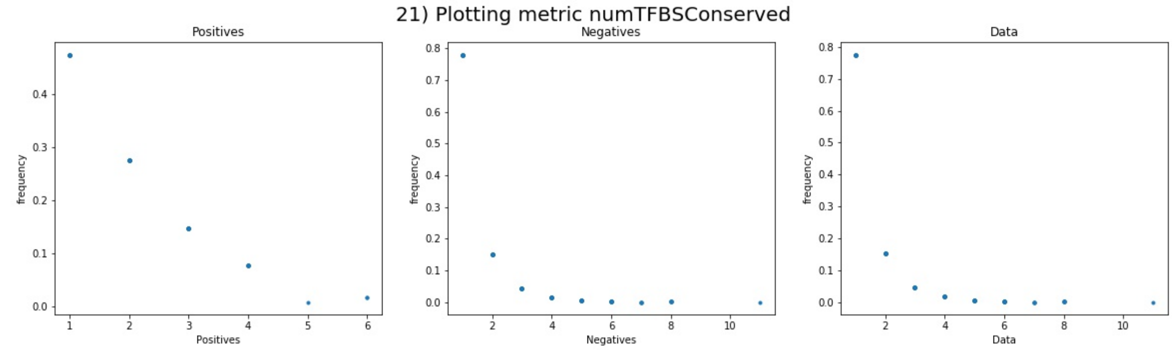

Figura 2.41: Sampling distribution of metric numTFBSConserved

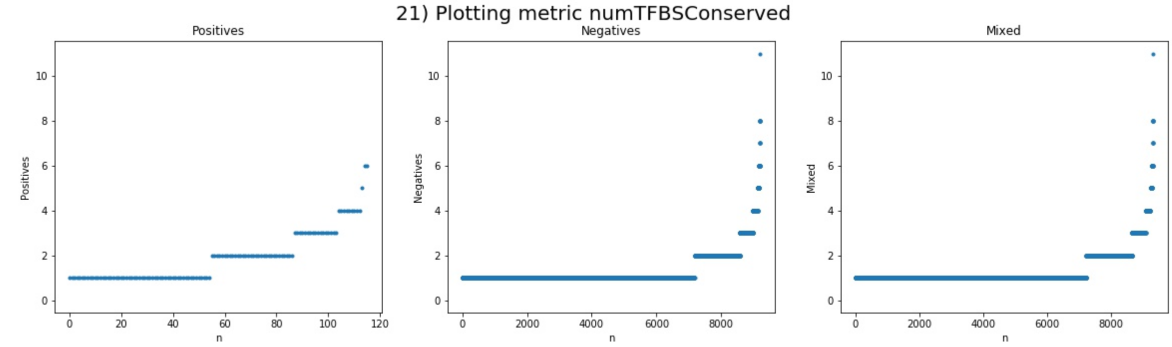

Figura 2.42: Values of metric numTFBSConserved

2.22 priPhastCons46way

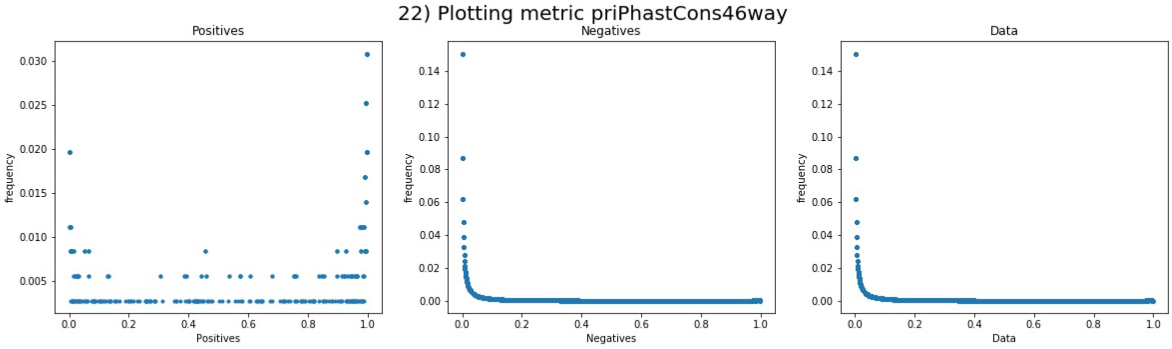

Figura 2.43: Sampling distribution of metric priPhastCons46way

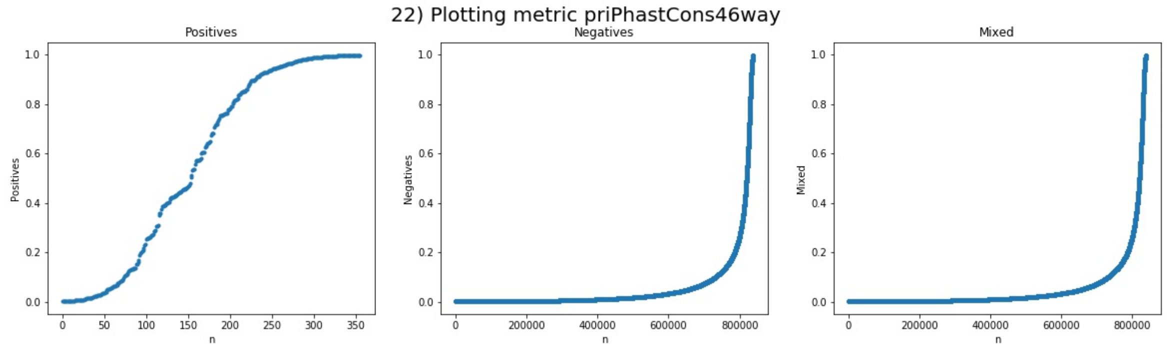

Figura 2.44: Values of metric priPhastCons46way

2.23 priPhyloP46way

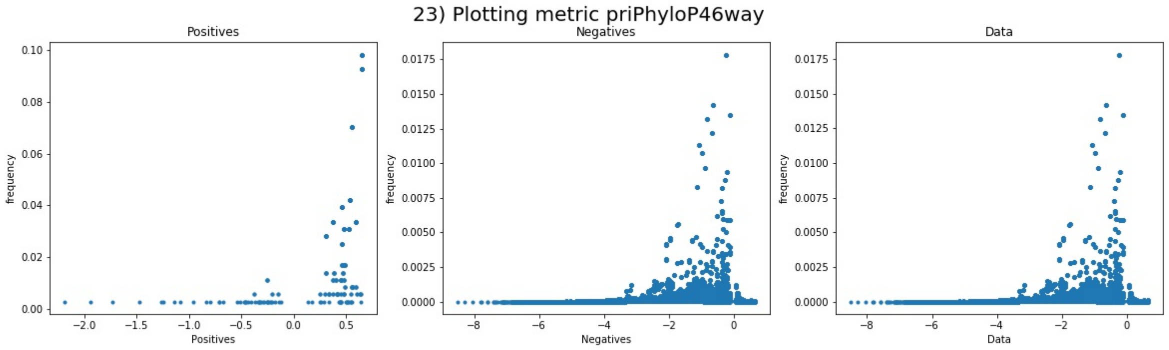

Figura 2.45: Sampling distribution of metric priPhyloP46way

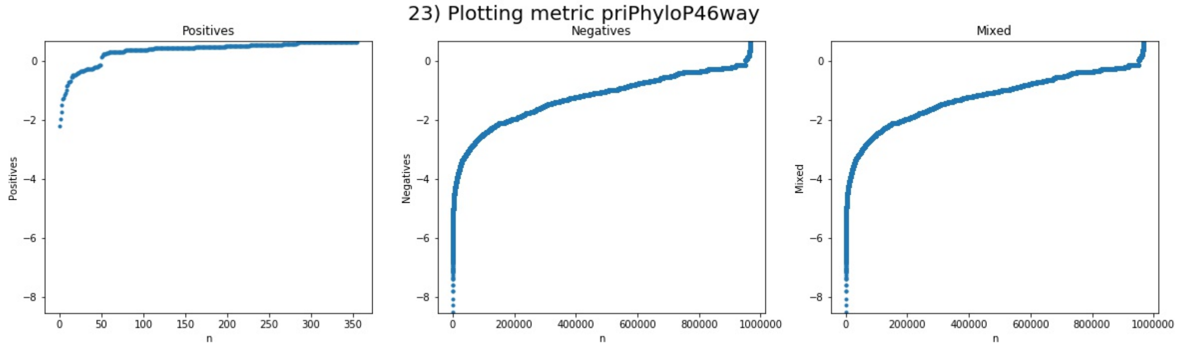

Figura 2.46: Values of metric priPhyloP46way

2.24 rareVar

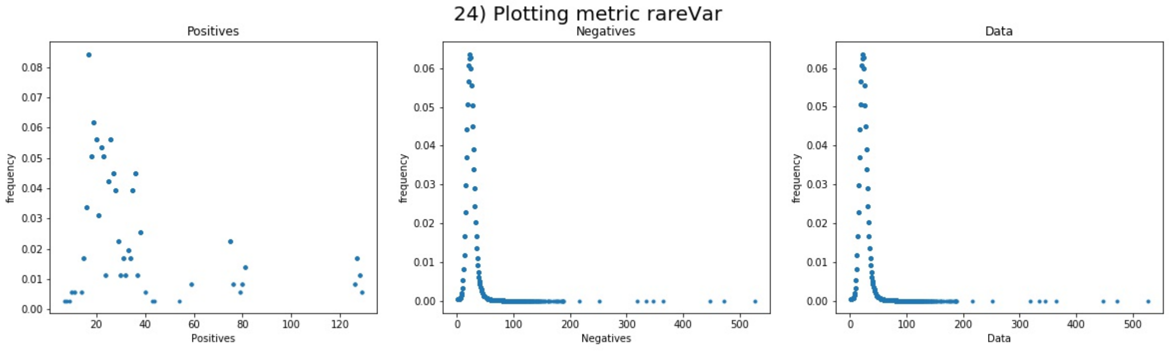

Figura 2.47: Sampling distribution of metric rareVar

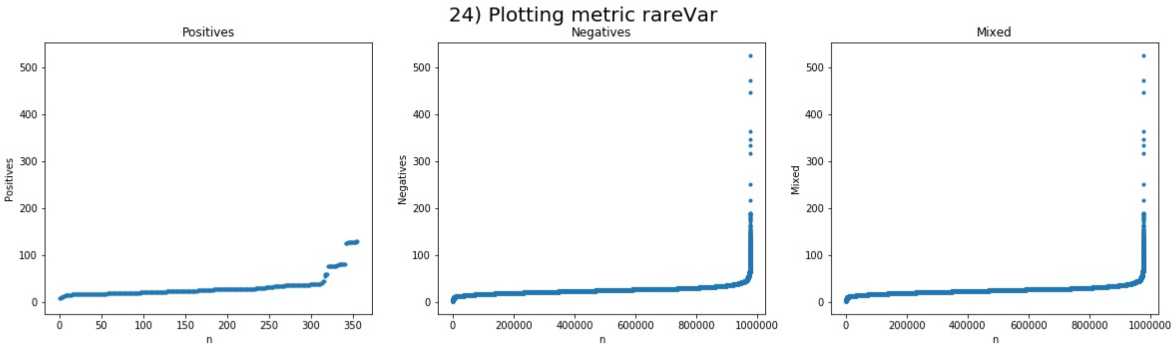

Figura 2.48: Values of metric rareVar

2.25 verPhastCons46way

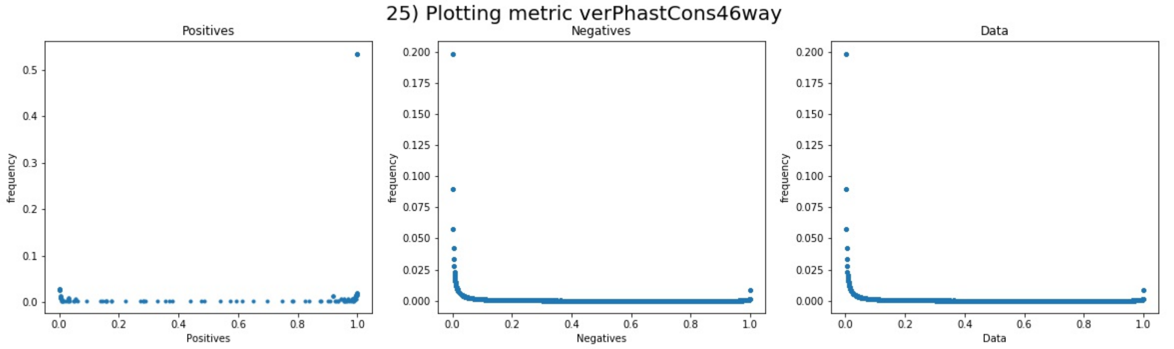

Figura 2.49: Sampling distribution of metric verPhastCons46way

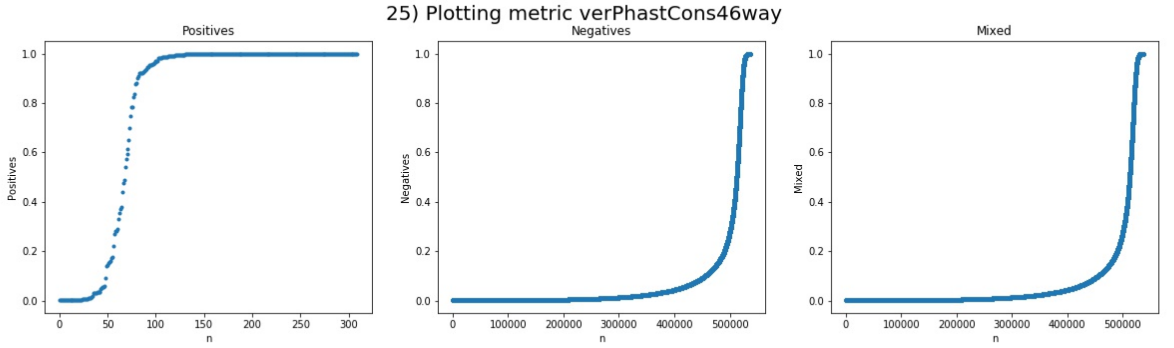

Figura 2.50: Values of metric verPhastCons46way

2.26 verPhyloP46way

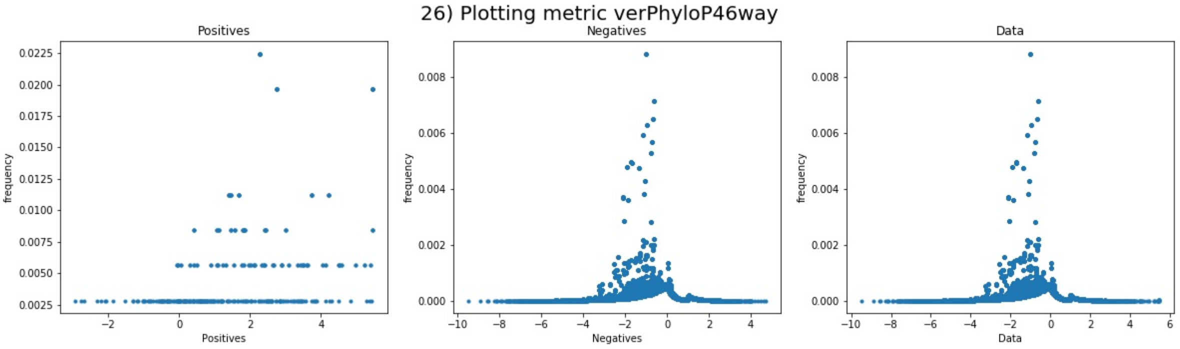

Figura 2.51: Sampling distribution of metric verPhyloP46way

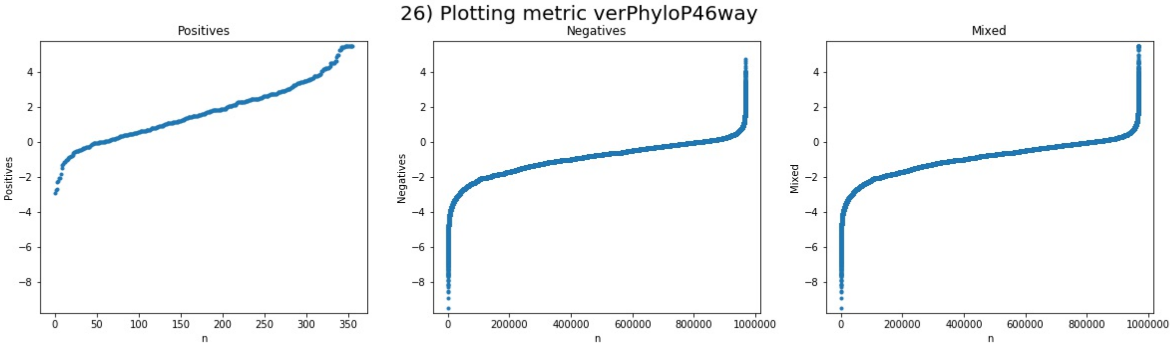

Figura 2.52: Values of metric verPhyloP46way

Parte II

Theory

3 Input modelling

3.1 Input values

The values used for each metric are the 3 following:

3.1.1 Normalized metric

Clearly one of the important metrics is the metric itself, that will be normalized to allow for input in $[0,1]$ range, zero mean and unary variance:

$$\text{metric}' = \frac{\text{metric} - \min\{\text{metric values}\}}{\max\{\text{metric values}\} - \min\{\text{metric values}\}}$$

(a) Input normalization to $[0,1]$ range

$$\text{metric}'' = \frac{\text{metric'} - \mathbb{E}\left(\{\}|\text{ metric' values}\right)}{\sqrt{\text{Var}\left(\text{metric' values}\right)}}$$

(b) Input normalization to zero mean and unary variance

3.1.2 Rarity

Another value we will be using in the input layer of the network is the rarity of the metric value, modelled as the surprise of extracting the given value from the estimated metric distribution extrapolated out of the sampling distribution.

If M is the estimated metric distribution and m is the value assumed by the metric in the given data point, we can model **rarity** as follows:

$$\text{rarity}(m) = 1 - M(m)$$

Figura 3.2: Rarity

3.1.3 Entropy

The third and final value used will be **entropy**, obtained using the estimated metric probability:

$$H(x) = -\mathbb{P}\left(x\right)\log\mathbb{P}\left(x\right)$$

Figura 3.3: Entropy

3.2 Feet

The input layer is comprised of 26 (number of metrics) *feet*, meaning tiny networks that are used to limit the initial linear combination of the metric input values to themselves.

Each feet is modelled as a locally connected dense layer.

3.3 Oversampling of positives

Since the positive values are just the 0.036% of the dataset we'll oversample these to weight more these values. Since the variance of positive data points is too high to extrapolate a distribution to generate significant new fuzzy data points, simple duplication will be used.

3.4 Undersampling of negatives

Since the negative values are more than the 99.96% of the dataset we'll undersample these to weight less these values.

3.5 Absence of information

Absence of information about a given metric will be modelled as **zeros**, meaning all values relative to the given absent metric for that data point will be treated as zero.

4 Output modelling

The output layer of the neural network is modelled by two neurons, one representing the positive class and one the negative class.

5 Weight initialization

5.1 Gaussian noise initialization

6
Locally connected dense layers

6.1 Leaky RELU

7 Dense layers

7.1 SELU

7.2 Drop out

Parte III

Code