# Cluster-Specific Baseline Correction in GC-IMS Data

Tecla Duran Fort

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## Contents

## 0. Preprocessing

### 0.1. Setup

Enable or disable parallelization based on the need for detailed error reporting or faster execution.

### 0.2. Dataset Creation

Creation of the dataset from the specified directory and files.

```r
# Create annotations dataframe
samples_directory <- "/storage/projects/TargetML/Urine_Pool"
annotations <- read.csv(file.path(samples_directory, "annotations.csv"))
annotations <- annotations[which(annotations$Class=="Urine_pool"),]

# Create GCIMS dataset object
urine <- GCIMSDataset$new(
  annotations,
  base_dir = samples_directory,
  on_ram = FALSE)
urine
```

### 0.3. Pre-process

Pre-processing steps include filtering, smoothing, and decimating the data to prepare it for further analysis.

```r
# Filter by Drift Time (Dt)
filterDt(urine, dt = c(5, 17)) # in ms
```

```
# Smooth the data
smooth(urine, rt_length_s = 3, dt_length_ms = 0.14)

# Decimate the data to reduce size
decimate(urine, rt_factor = 1, dt_factor = 2)
urine$realize()
```

## 0.4. Alignment

Alignment of the samples based on the reference sample to standardize the data across different runs.

```
reference <- 104
align(urine, reference_sample_idx = reference, align_dt = TRUE,
      align_ip = TRUE, method_rt = "none")
align(urine, reference_sample_idx = reference, align_dt = FALSE,
      align_ip = FALSE, method_rt = "ptw", ploynomial_order= 2)
urine$realize()

# PTW adjustment to correct small mismatches in sample dimensions
filterDt(urine, dt_range = c(min(dtime(urine)),max(dtime(urine))))
filterRt(urine, rt_range = c(min(rtime(urine)),max(rtime(urine))))
```

Further alignment using a new method to ensure accurate peak detection.

```
# Align using new method with specified parameters
percentage_movement <- 0.2
align_pks_ds(urine, 104, percentage_movement)
urine$realize()
filterDt(urine, dt = c(5, 14)) # in ms
```

## 0.5. Peak Detection and Clustering

Peak detection and clustering to identify significant features in the data.

```
findPeaks(
  urine,
  rt_length_s = 3,
  dt_length_ms = 0.14,
  verbose = TRUE,
  dt_peakwidth_range_ms = c(0.15, 0.4),
  rt_peakwidth_range_s = c(10, 25),
  dt_peakDetectionCWTParams = list(exclude0scaleAmpThresh = TRUE),
  rt_peakDetectionCWTParams = list(exclude0scaleAmpThresh = TRUE),
  dt_extension_factor = 0,
  rt_extension_factor = 0,
  exclude_rip = TRUE,
  iou_overlap_threshold = 0.2
)
peak_list <- peaks(urine)
```

```
peak_clustering <- clusterPeaks(
  peak_list,
  distance_method = "euclidean",
  dt_cluster_spread_ms = 0.1,
  rt_cluster_spread_s = 20,
  clustering = list(method = "hclust")
)
peak_list_clustered <- peak_clustering$peak_list_clustered
```

Creating and refining the peak table to include only relevant peaks based on their representation across the samples.

```
integratePeaks(
  urine,
  peak_clustering$peak_list,
  integration_size_method = "fixed_size",
  rip_saturation_threshold = 0.1
)
peak_list <- peaks(urine)
peak_table <- peakTable(peak_list, aggregate_conflicting_peaks = max)
```

## 0.6. Removing Underrepresented Clusters

Removing underrepresented clusters to maintain data reliability.

```
# Count non-NA values per cluster and determine their percentage representation
counts <- peak_table$peak_table %>%
  mutate(Count = rowSums(!is.na(across(-cluster)))) %>%
  select(cluster, Count)

counts <- counts %>%
  mutate(Percentage = (Count / nrow(annotations)) * 100)

threshold <- 25

selected_clusters <- counts %>%
  filter(Percentage > threshold) %>%
  pull(cluster)

peak_list <- peak_list %>% filter(cluster %in% selected_clusters)
peak_table <- peakTable(peak_list, aggregate_conflicting_peaks = max)
```

## 0.7. Impute Peak Table

In order to obtain a complete peak table with values for all clusters across all samples, we apply the function `imputePeakTable()`. This step fills in missing peak intensities by directly integrating the signal within the fixed Region of Interest (ROI) defined for each cluster, even in samples where no peak was originally detected.

The ROI coordinates used for imputation are stored in `cluster_stats`, which contains the consensus boundaries assigned during clustering. The result is a dense peak table where all clusters are consistently represented.

```
peak_table_imputed <- imputePeakTable(
  peak_table$peak_table_matrix,
  urine,
  peak_clustering$cluster_stats
)
```

# 1. Correcting Baseline Affecting The Peak Table

**Tecla**

In this section, we address the process of baseline correction, a crucial step in accurate peak quantification in GC-IMS data analysis. During peak integration, there is typically an overestimation of peak volume because the peak does not start from zero but has a certain background/baseline noise level. This overestimation can significantly impact subsequent analyses, either because the overestimation is not uniform across all peaks or, which is the actual case, it can lead to an exaggerated perception of peak stability. Although various baseline correction methods exist, this report focuses on removing this background by optimizing a window around each peak and assuming it constant (like an additive offset) within this window. This window is adjusted relative to the fixed size of the Region of Interest (ROI) to effectively contain and correct for the baseline noise.

## 1.1. Optimizing Patch Size for Baseline Removing

When detecting peaks in GC-IMS data, each peak is initially assigned **fixed drift and retention time limits** (`fixedsize_dt_min_ms`, `fixedsize_dt_max_ms`, `fixedsize_rt_min_s`, `fixedsize_rt_max_s`), which is common in all the peaks belonging to the same cluster. However, these predefined ranges might not fully capture the **baseline intensity**, which is needed for proper signal correction.

We want to determine **how much to expand the peak detection range** to ensure that the **baseline is included**, but **without making it larger than necessary**.

- **The baseline is reached when the intensity stabilizes** (i.e., it stops decreasing with expansion).
- **A smaller patch is preferable**, as we assume the baseline is constant and larger patches could introduce unwanted variability.

Instead of taking the **minimum intensity**, we compute the **median of the lowest 10% of intensity values** using `quantile()` function. This provides a more robust estimation of the baseline.

Additionally, if the computed **MinValue is negative**, it is set to **0** to avoid unrealistic values (it actually happens in one of the clusters).

### Functions

#### `extractMinValues`

- Iterates through all samples and retrieves their detected peaks.
- Expands the peak's drift and retention time ranges by `ampliation`.
- Extracts the intensity values in this **expanded patch** and computes the **median of the lower 10% quantile** `quantile(patch, 0.05)`.
- **Ensures MinValue is not negative** (sets negative values to 0).
- Returns `peak_list` with an updated `MinValue` column.

#### `extractMinValues_2`

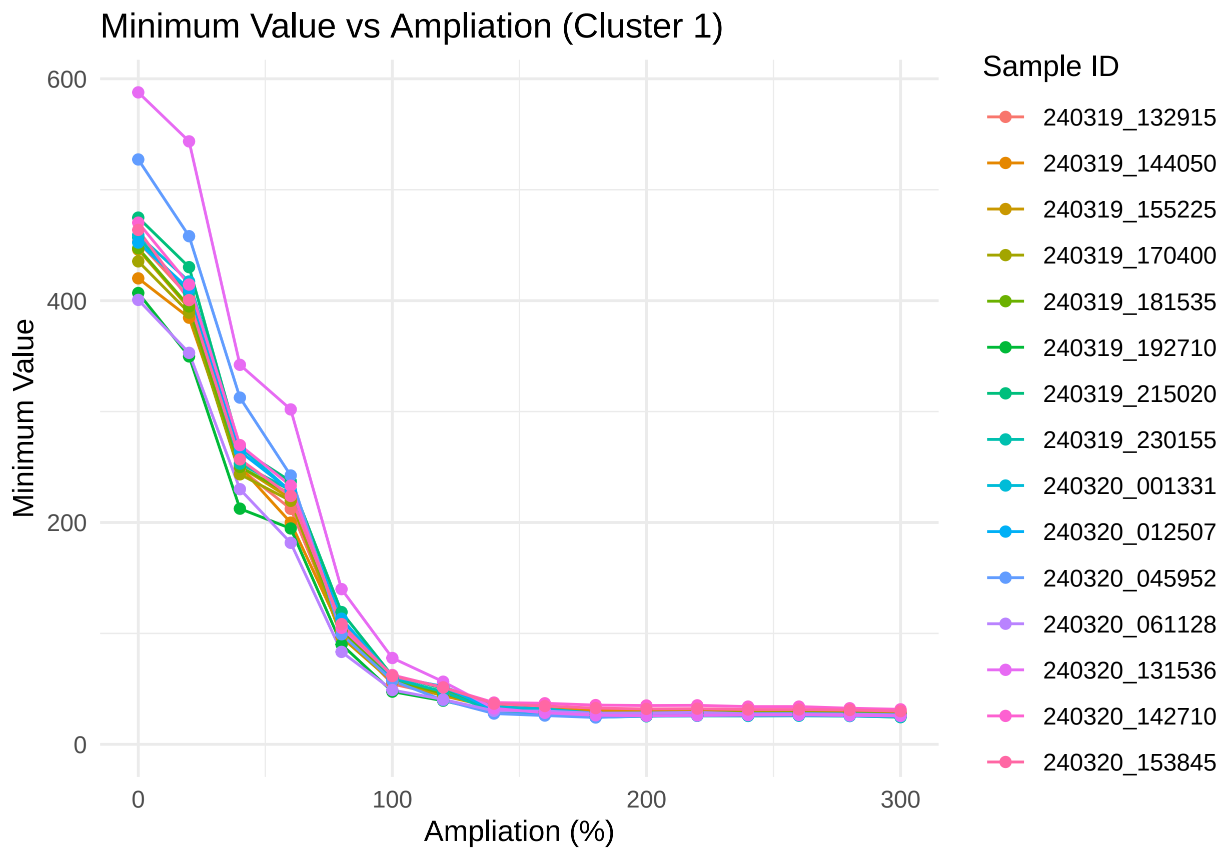
- Works similarly but focuses on a **specific cluster** and a set number of samples (`n_samples`).
- Returns a **vector of MinValues**, without modifying `peak_list`.

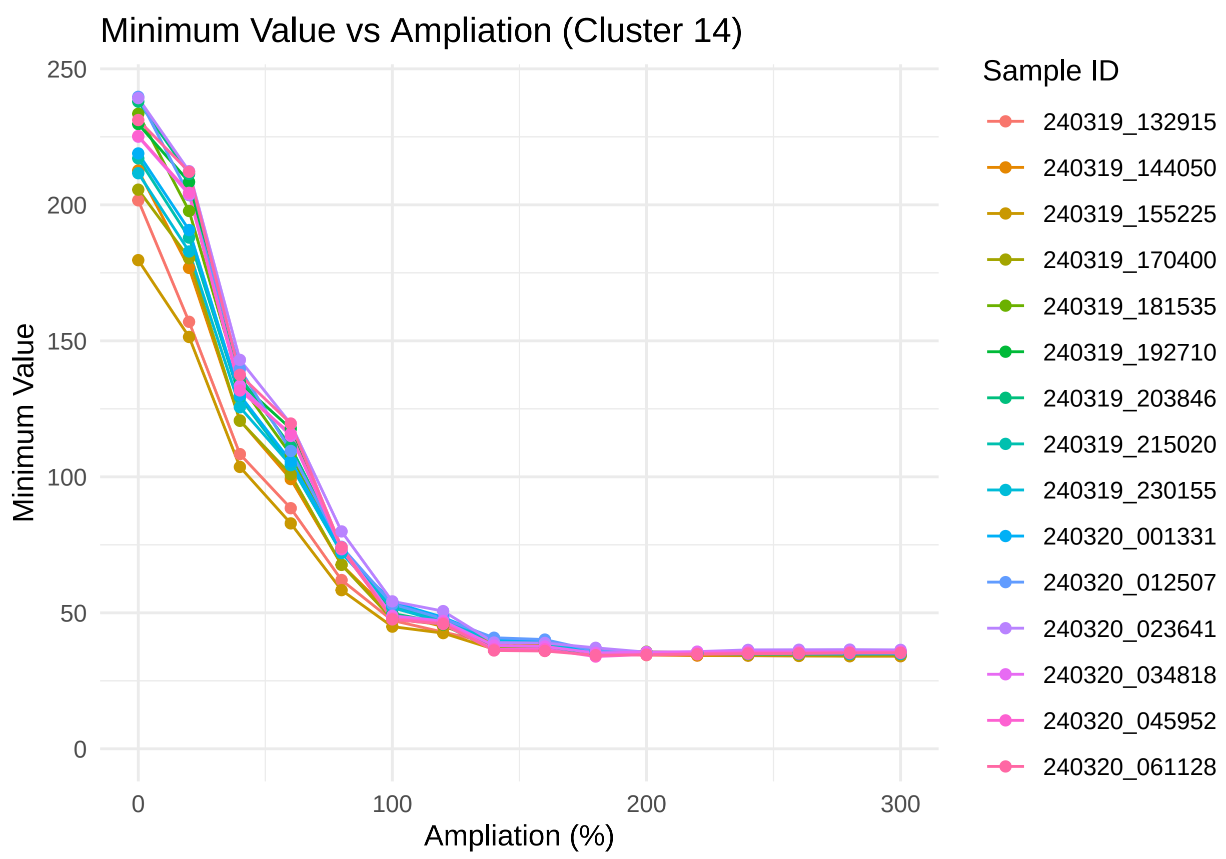
### Plot

- **X-axis:** Expansion percentage (`ampliation`).
- **Y-axis:** Baseline intensity (median of lower decile, with no negative values).
- **Lines:** Each sample's intensity evolution.

By analyzing these curves, we identify the **minimum necessary expansion** to capture the baseline **without excessive enlargement**.

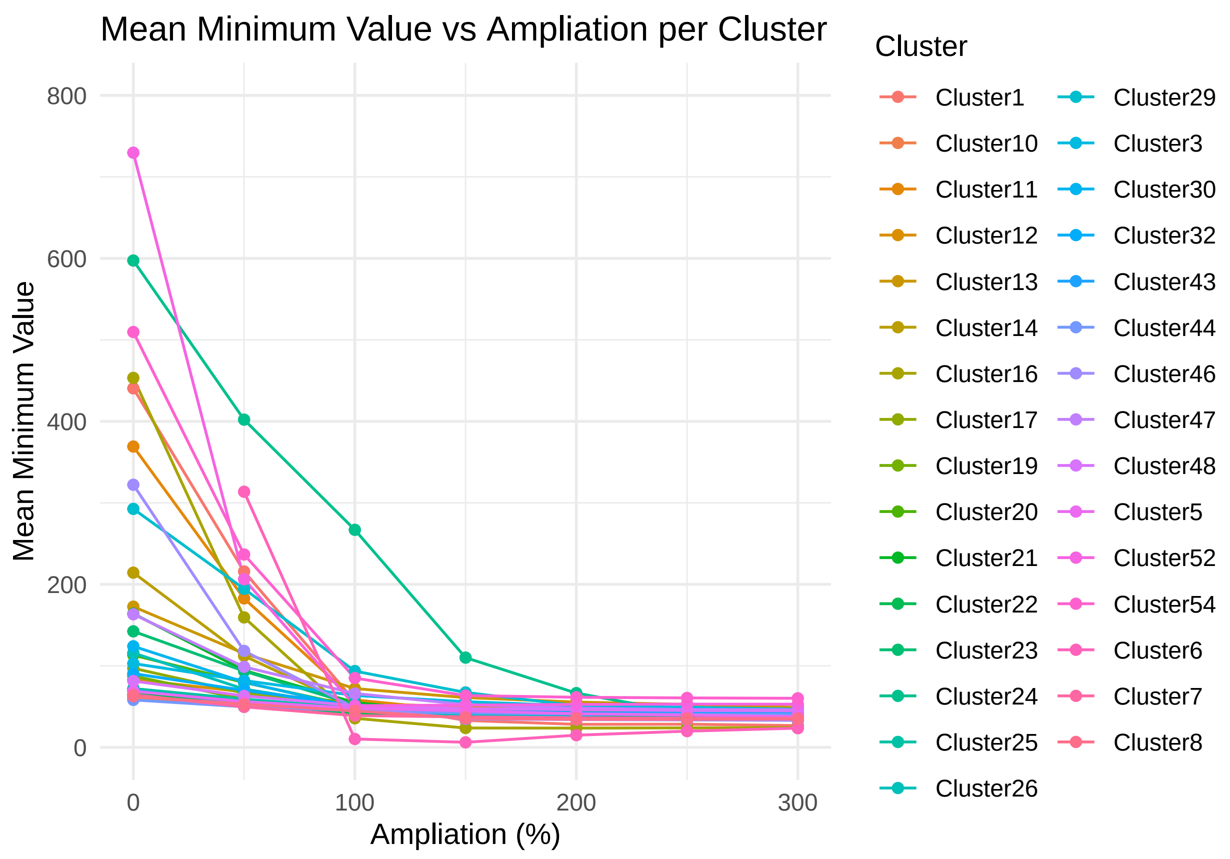
**Visualisation In Specific Clusters**





Minimum Value vs Ampliation (Cluster 14)
Minimum Value
Ampliation (%)
250
200
150
100
50
0
0
100
200
300
Sample ID
240319_132915
240319_144050
240319_155225
240319_170400
240319_181535
240319_192710
240319_203846
240319_215020
240319_230155
240320_001331
240320_012507
240320_023641
240320_034818
240320_045952
240320_061128

**Deciding a common ampliation**



Based on these plots, we will adopt the **200%** ampliation value (i.e., double the size of the ROI), as most clusters appear to have stabilized at a value that we will consider the baseline.

## 1.2. Correcting Baseline

During peak integration in GC-IMS data, a rectangular Region of Interest (ROI) is used to quantify the signal associated with each peak. However, the signal within this region may include a contribution from the baseline, which can lead to overestimated peak volumes.

To correct this effect, we implement a baseline correction that estimates the background signal for each cluster and subtracts it from the imputed peak table. Although all steps are available as a standalone function (`correctBaseline()`), we first describe the full procedure in detail.

### 1.2.1. Calculating Fixed Size Area

During GC-IMS data analysis, each detected peak initially has its own boundaries in retention time (rt) and drift time (dt). However, when peaks are clustered using `clusterPeaks()`, a consensus Region of Interest (ROI) is defined for each cluster.

If the `integration_size_method = "fixed_size"` is selected, this fixed-size ROI is applied uniformly to all samples when integrating the signal of that cluster — even if the individual peak shapes or positions vary.

To estimate how much of the integrated volume may come from baseline signal, we compute the *fixedsize_Area* of each ROI, which is common to all peaks of the same cluster:

```
fixedsize_Area = (fixedsize_dt_max_ms - fixedsize_dt_min_ms) × (fixedsize_rt_max_s - fixedsize_rt_min_s
peak_list <- peak_list %>%
  mutate(
    fixedsize_Area = (fixedsize_dt_max_ms - fixedsize_dt_min_ms) * (fixedsize_rt_max_s - fixedsize_rt_m
  )
```

This area is used to convert the estimated baseline intensity into a volume contribution (intensity × area), which is then subtracted from the imputed peak table.

Note: The existing `Area` column in the `peak_list` shows the size of each individual peak's rectangle. When using the `fixed_size` method, integration is done over a common rectangle per cluster, so `Area` does not match the region actually used for integration.

### 1.2.2. Estimating the Residual Volume

Once we have the fixed-size area, we estimate the residual volume — the portion of signal attributable to the baseline — for each cluster in each sample. This is done using the function `computeResidualVolume()`, which performs the following steps:

- **Iterates through all clusters and samples**.
- **Expands** the fixed integration region by a given percentage (`ampliation`) to capture more surrounding baseline.
- **Extracts** the intensity values from the expanded region and computes the median of the lowest 10% (5th percentile).
- If no peak is detected in a given sample, it falls back to using global `cluster_stats` information to define the ROI.
- **Multiplies** the estimated background intensity by the fixed-size area to compute the residual volume.
- Returns a matrix-like dataframe with residual volume values for each cluster-sample pair.

```
residual_volume_df <- computeResidualVolume(
  dataset = urine,
  peak_list = peak_list,
  cluster_stats = peak_clustering$cluster_stats,
  ampliation = 200
)
residual_volume_df <- as.data.frame(t(residual_volume_df))
```

### 1.2.3. Correcting the Peak Table

We now apply the baseline correction by subtracting the residual volumes from the peak table:

```
peak_table_imputed_df <- as.data.frame(peak_table_imputed)
peak_table_corrected <- peak_table_imputed_df - residual_volume_df
```

### 1.2.4. Full Correction with `correctBaseline()`

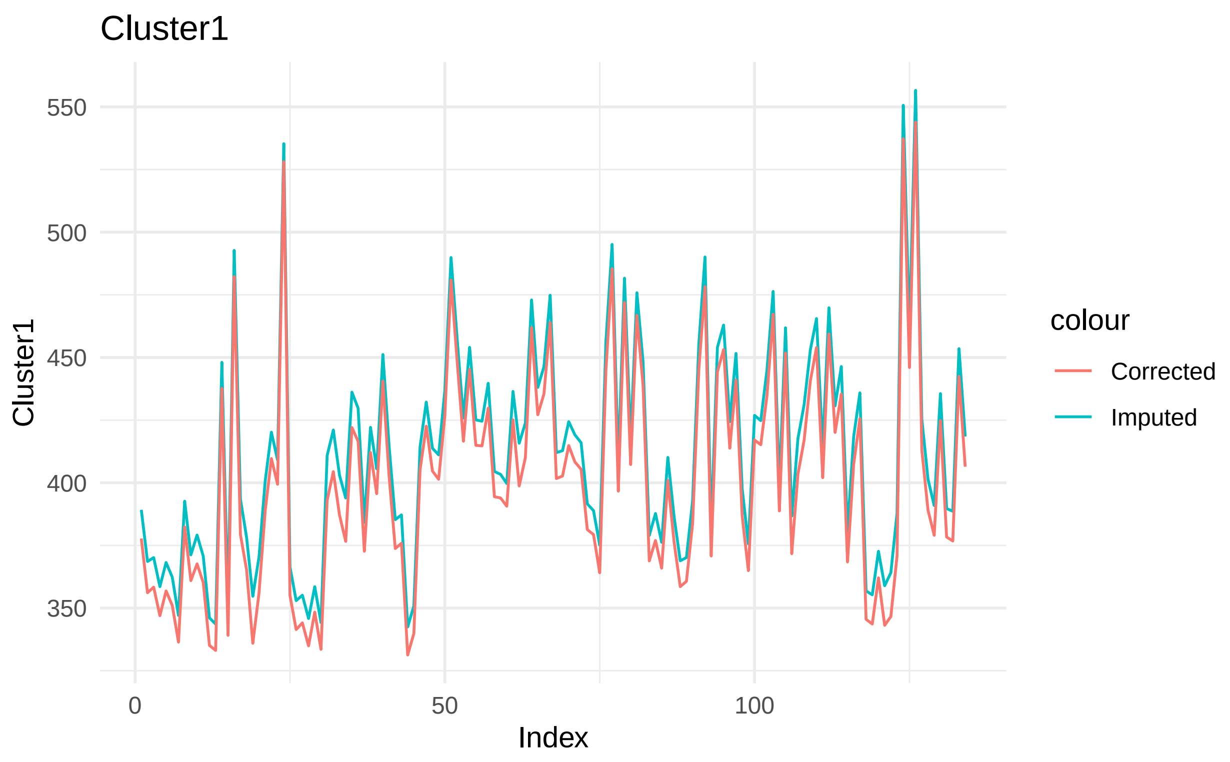
To simplify and reproduce the full baseline correction workflow, all the steps above can be executed in a single function:

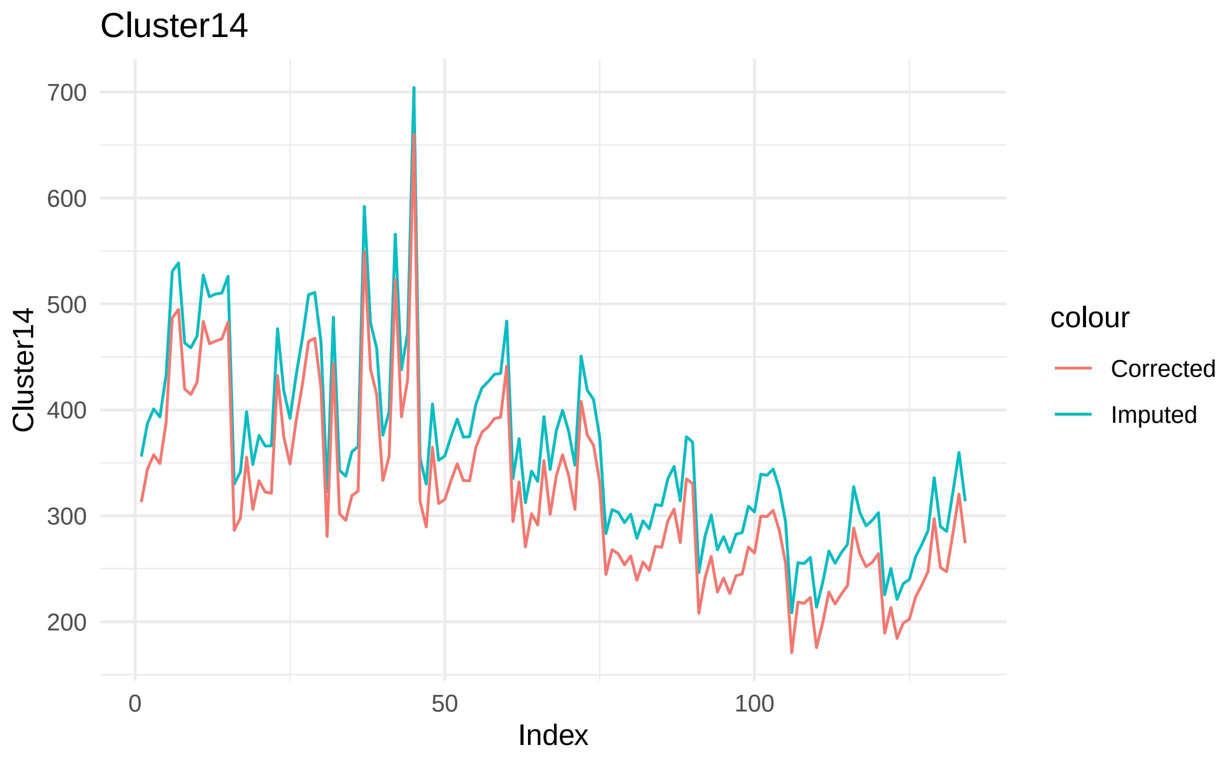
```
peak_table_corrected <- correctBaseline(
  dataset = urine,
  peak_list = peak_list,
  cluster_stats = peak_clustering$cluster_stats,
  ampliation = 200
)
```

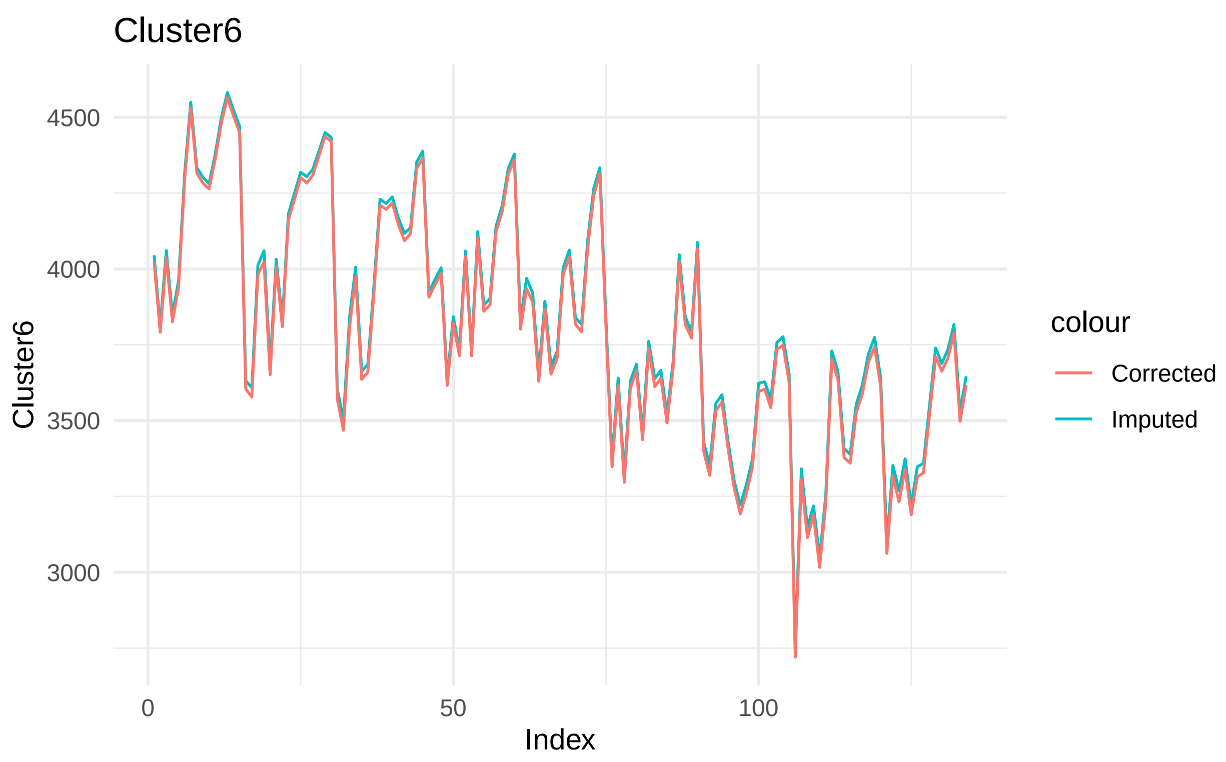
This function internally performs the fixed-size area calculation, residual volume estimation, imputation, and subtraction.

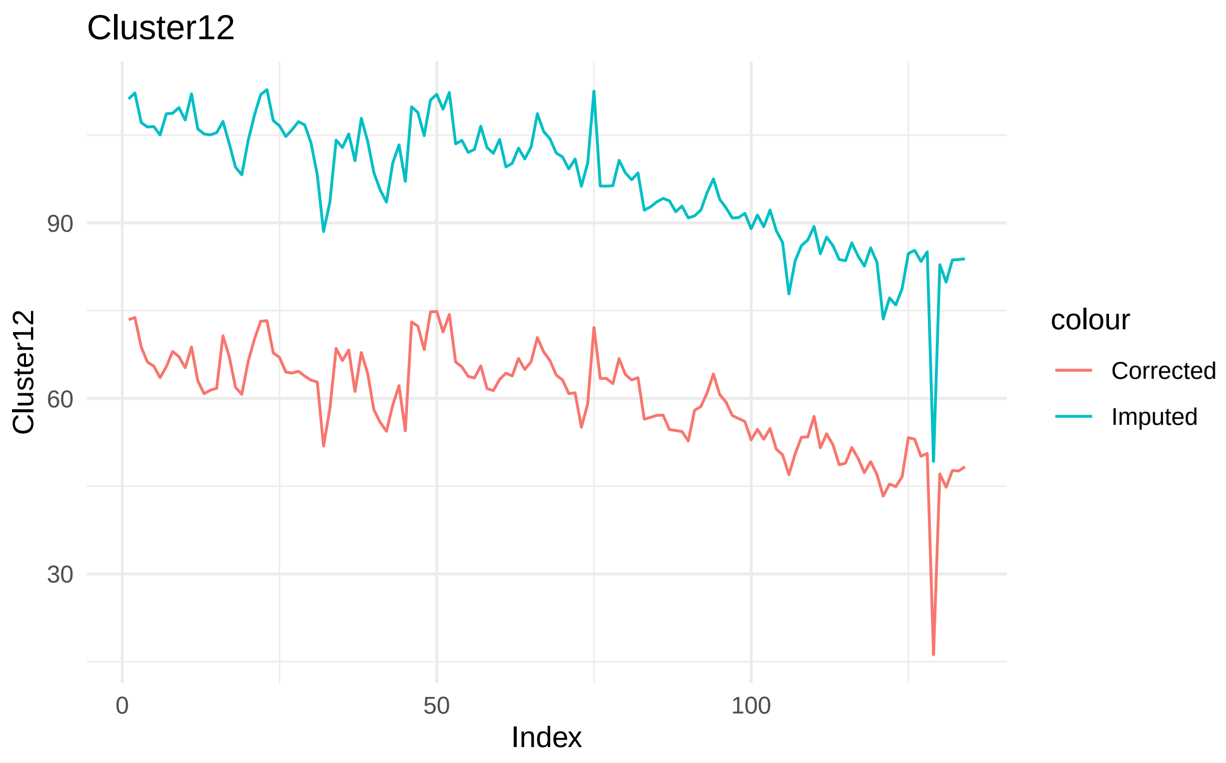
#### 1.2.5. Visualizing the Effect of Baseline Correction

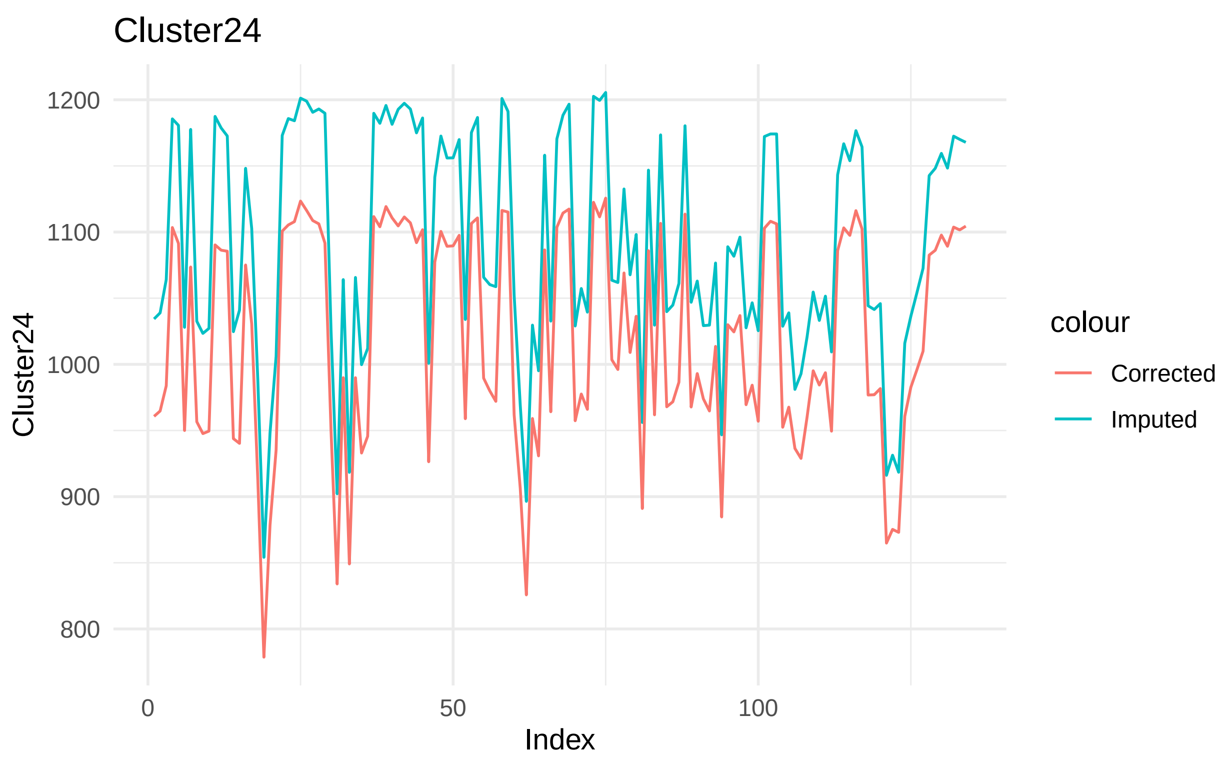
We can compare the imputed vs. baseline-corrected values across clusters:



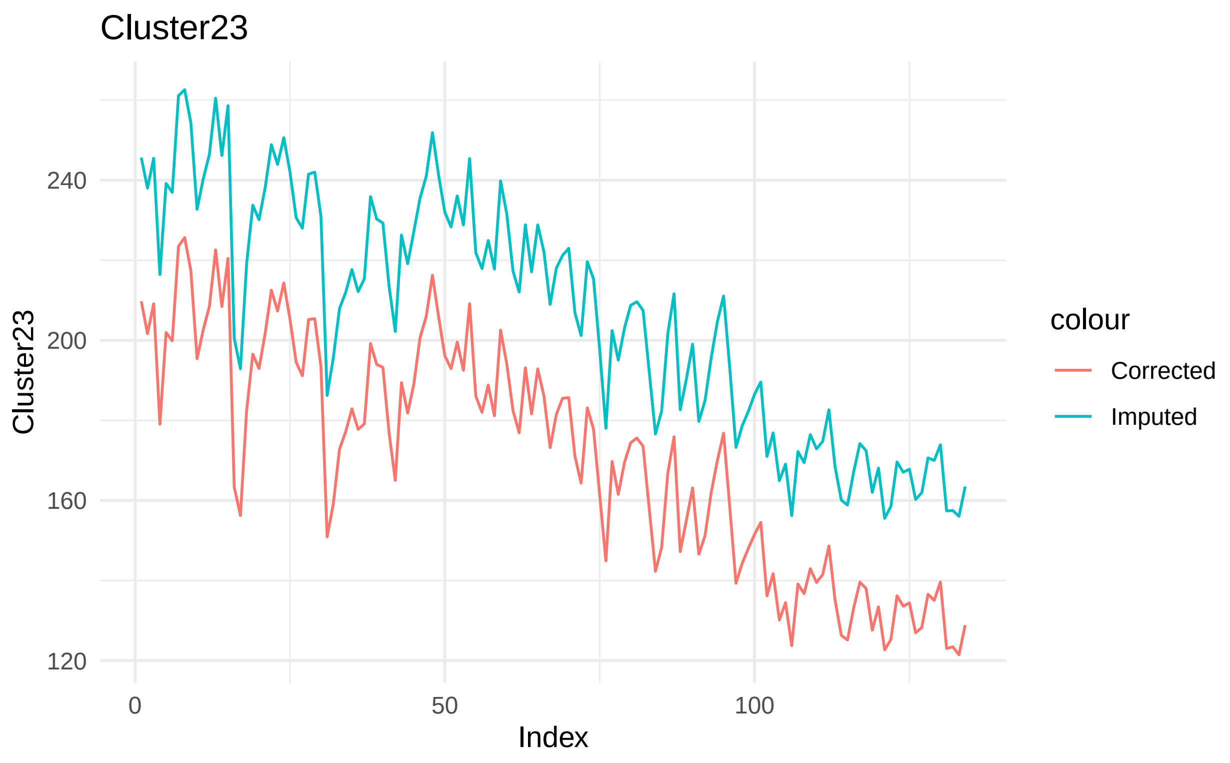



Cluster6
4500
4000
3500
3000
Cluster6
0
50
100
Index
colour
Corrected
Imputed

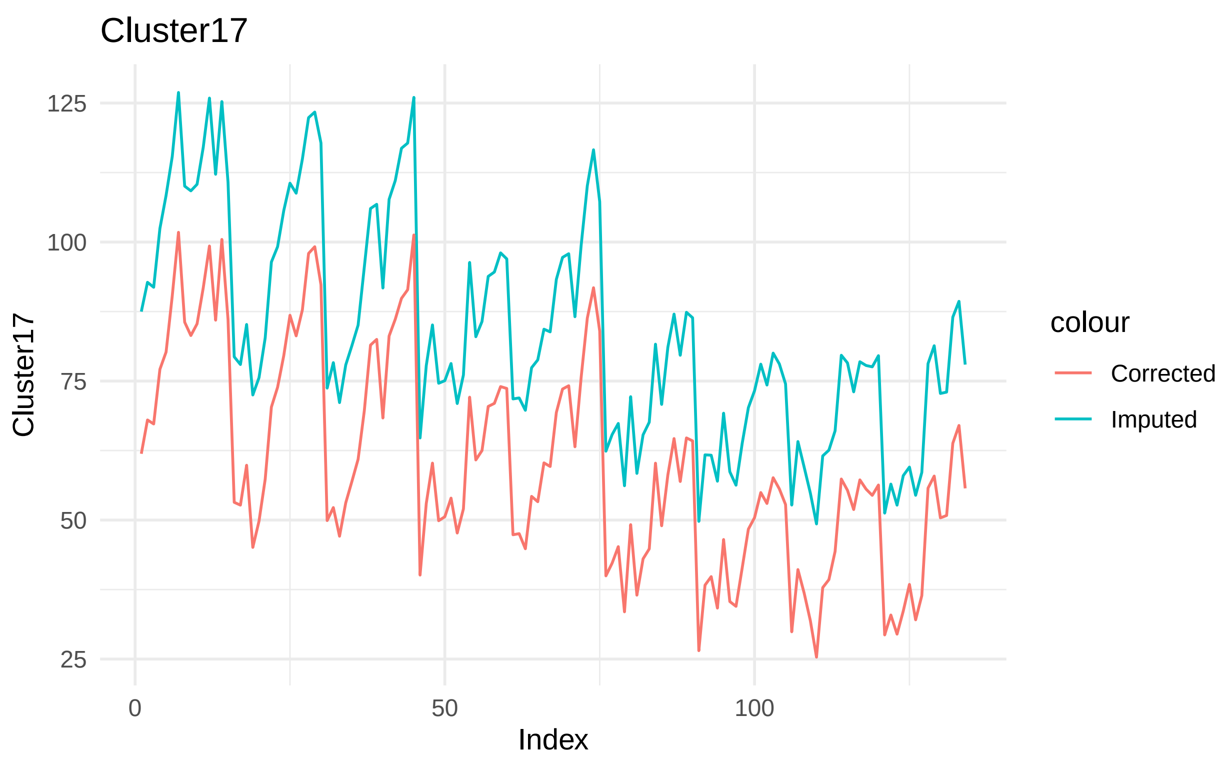

Cluster12
90
60
30
Cluster12
0
50
100
Index
colour
Corrected
Imputed

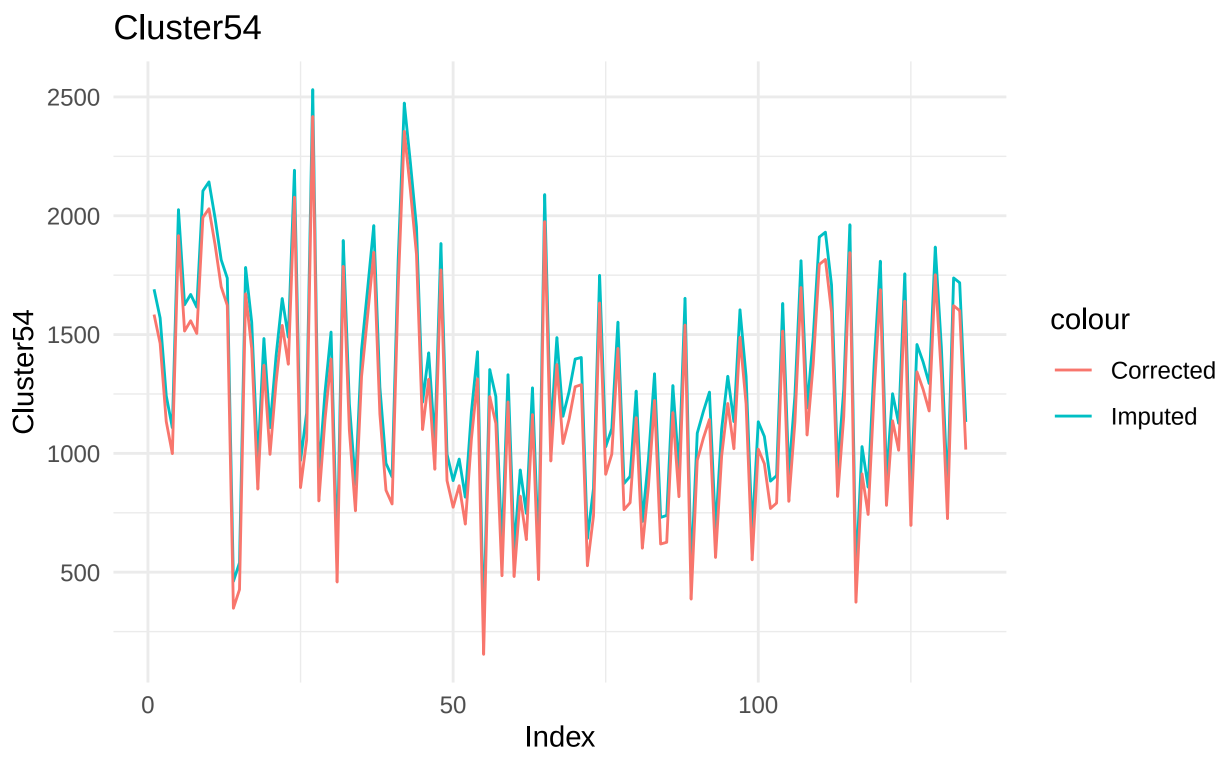


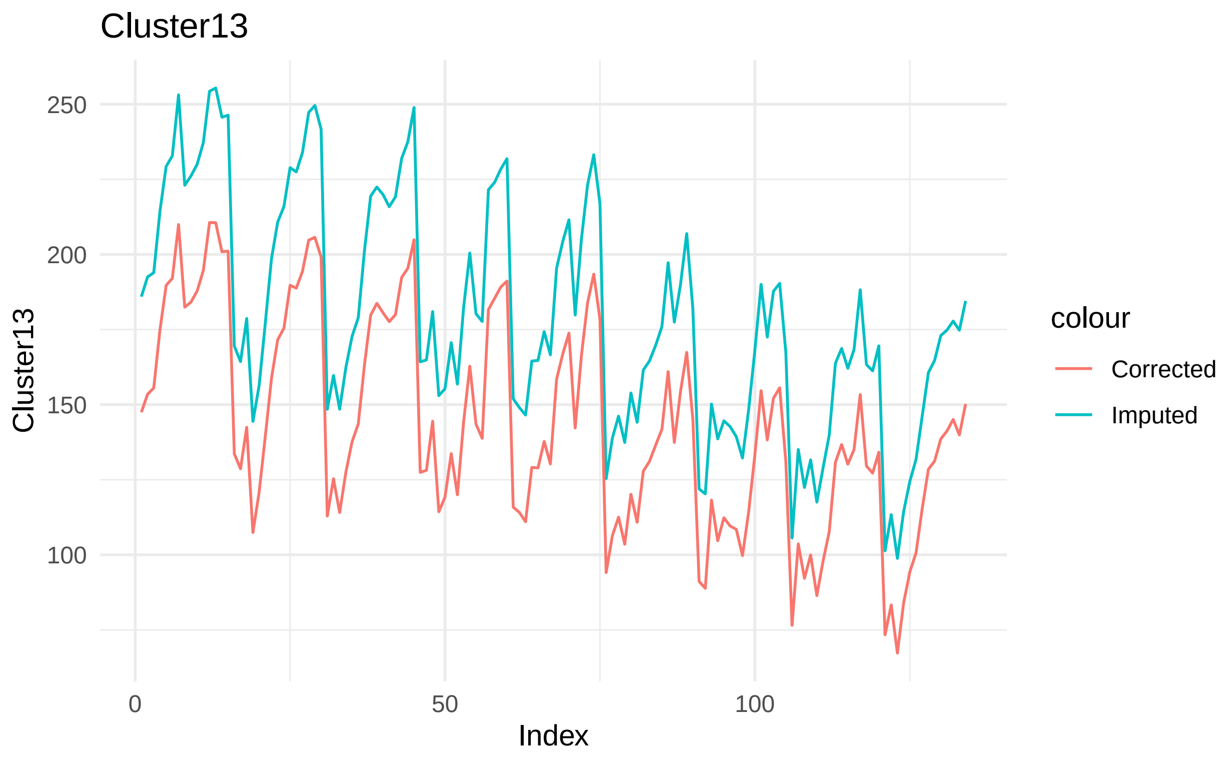
Cluster24
1200
1100
1000
900
800
Cluster24
0
50
100
Index
colour
Corrected
Imputed

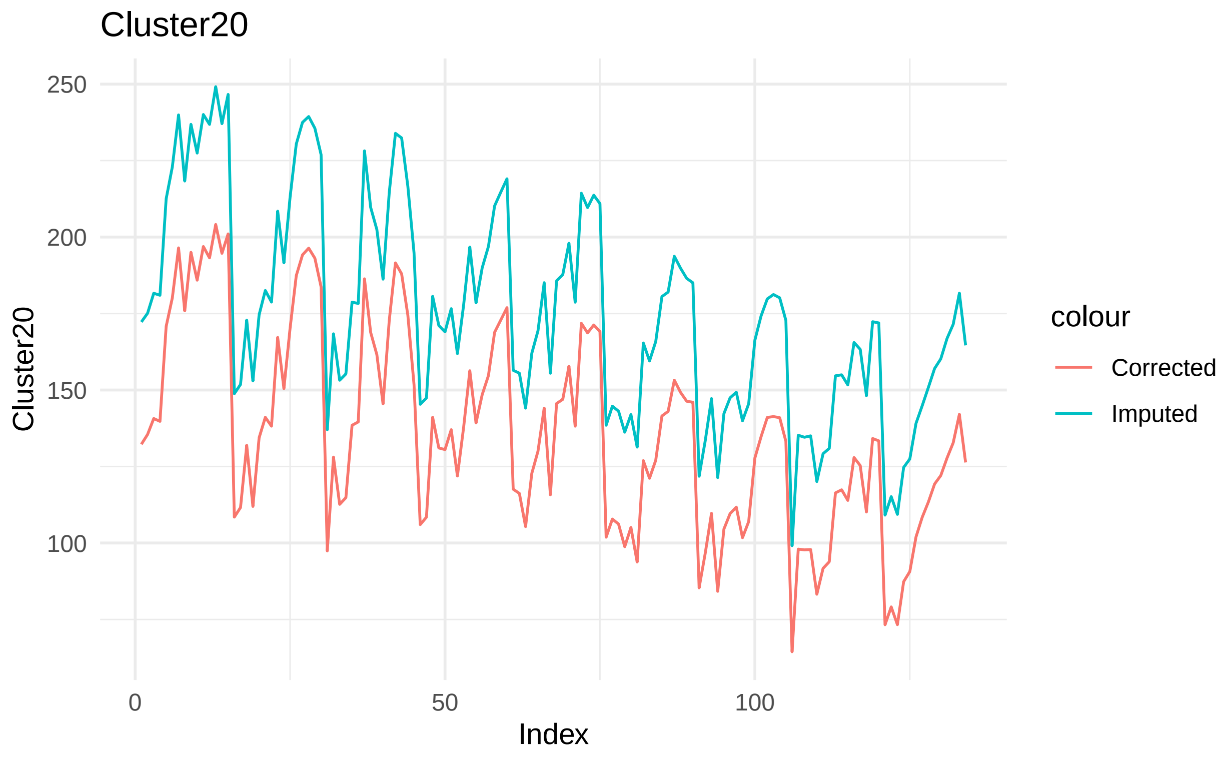


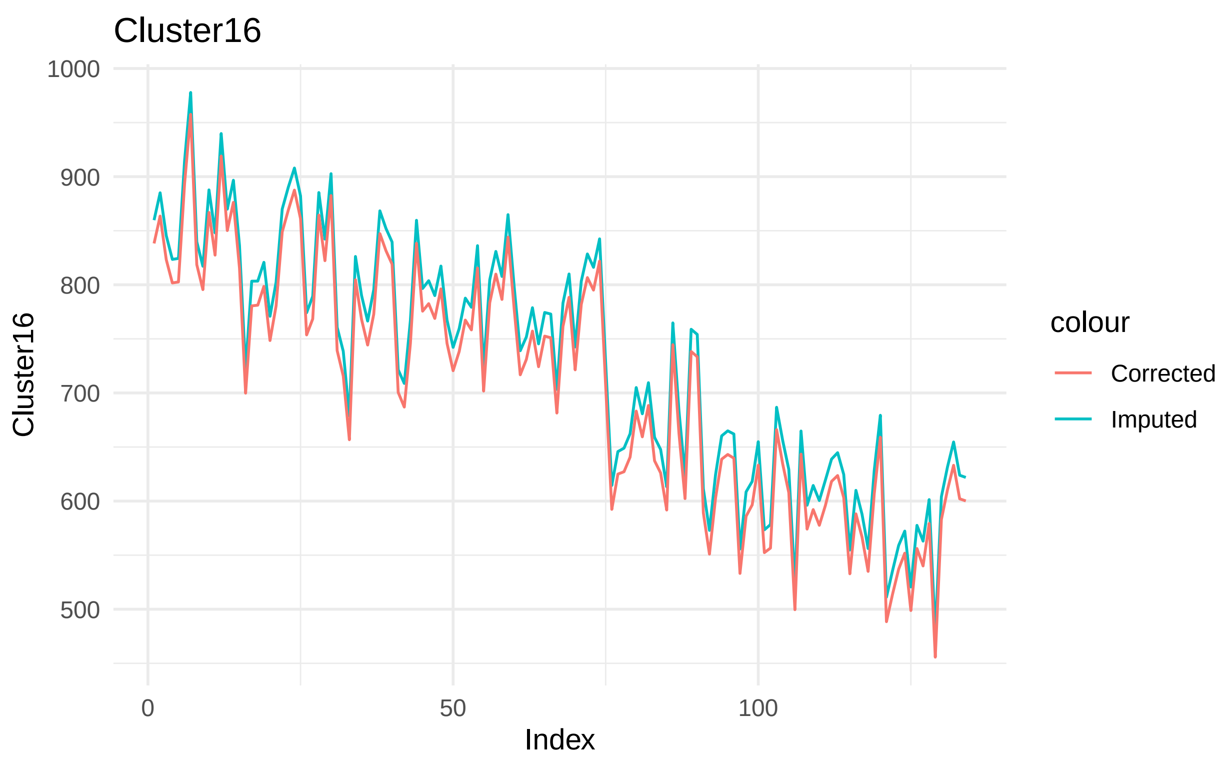
Cluster23
240
200
160
120
Cluster23
0
50
100
Index
colour
Corrected
Imputed

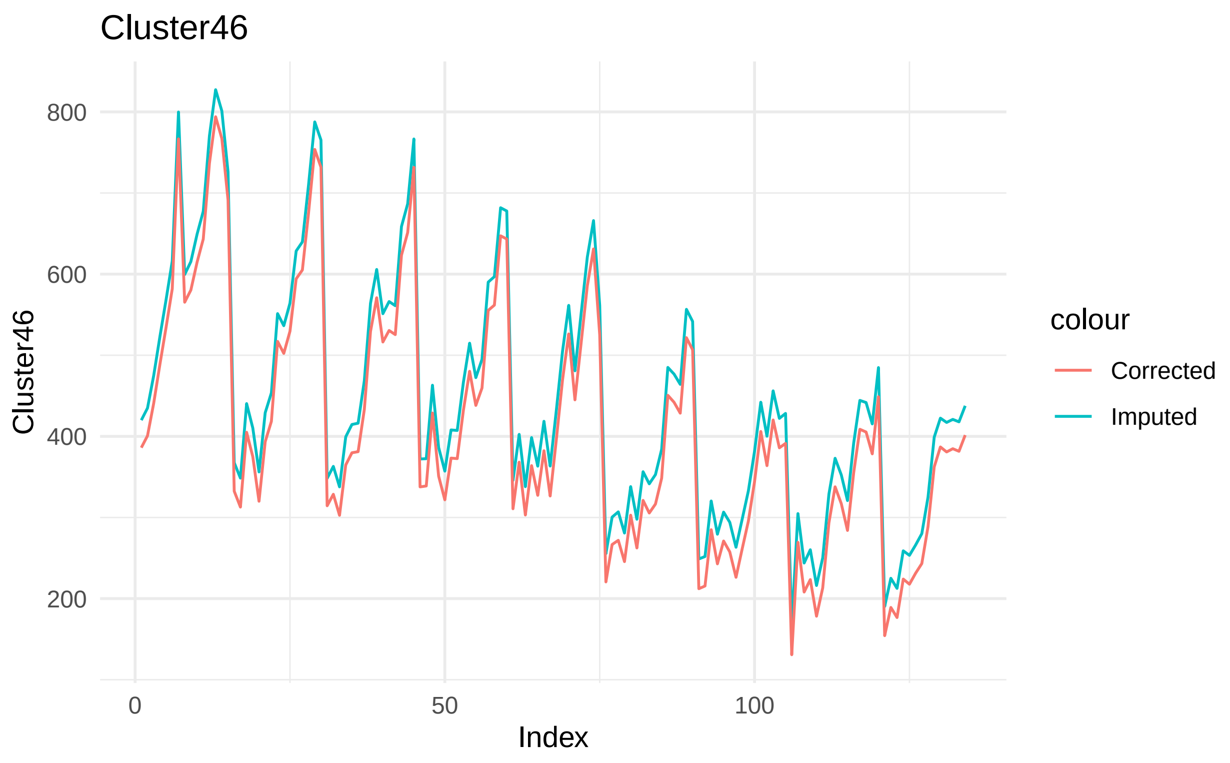

Cluster17
125
100
75
50
25
Cluster17
0
50
100
Index
colour
Corrected
Imputed

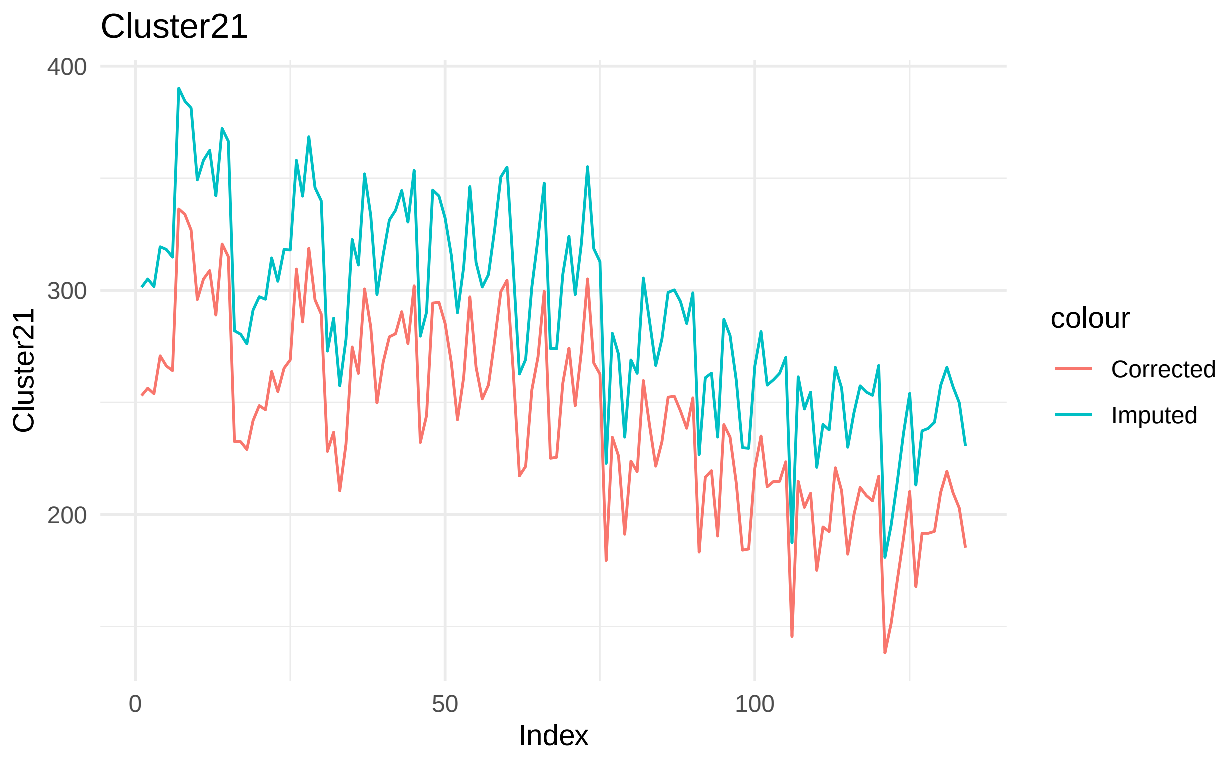

Cluster54
2500
2000
1500
1000
500
Cluster54
0
50
100
Index
colour
Corrected
Imputed

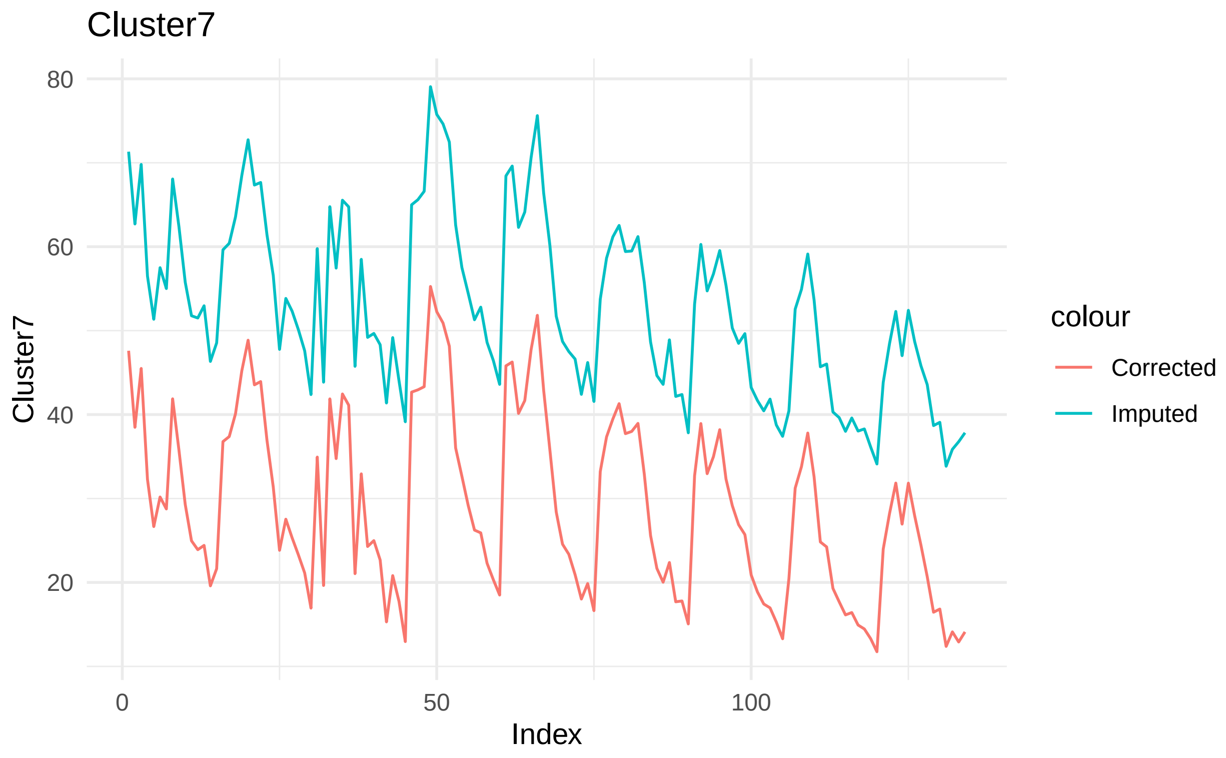

Cluster13
250
200
150
100
Cluster13
0
50
100
Index
colour
Corrected
Imputed

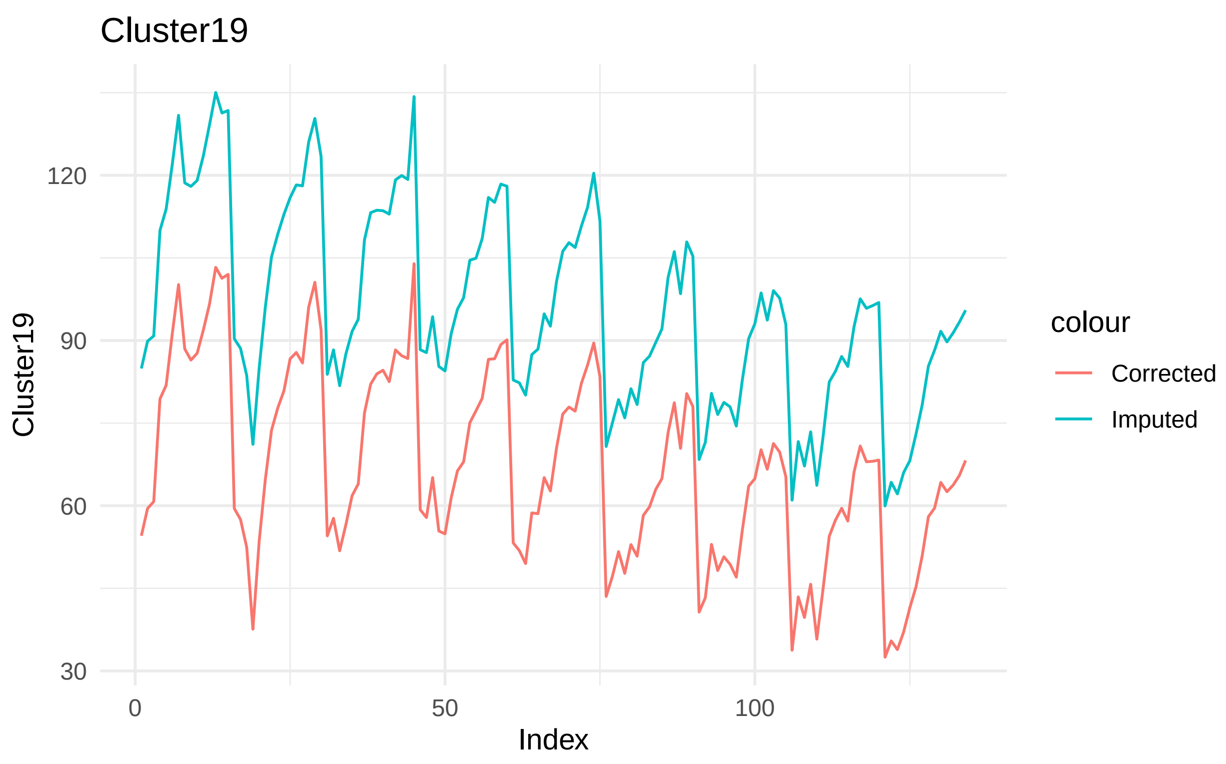

Cluster20
250
200
150
100
Cluster20
0
50
100
Index
colour
Corrected
Imputed

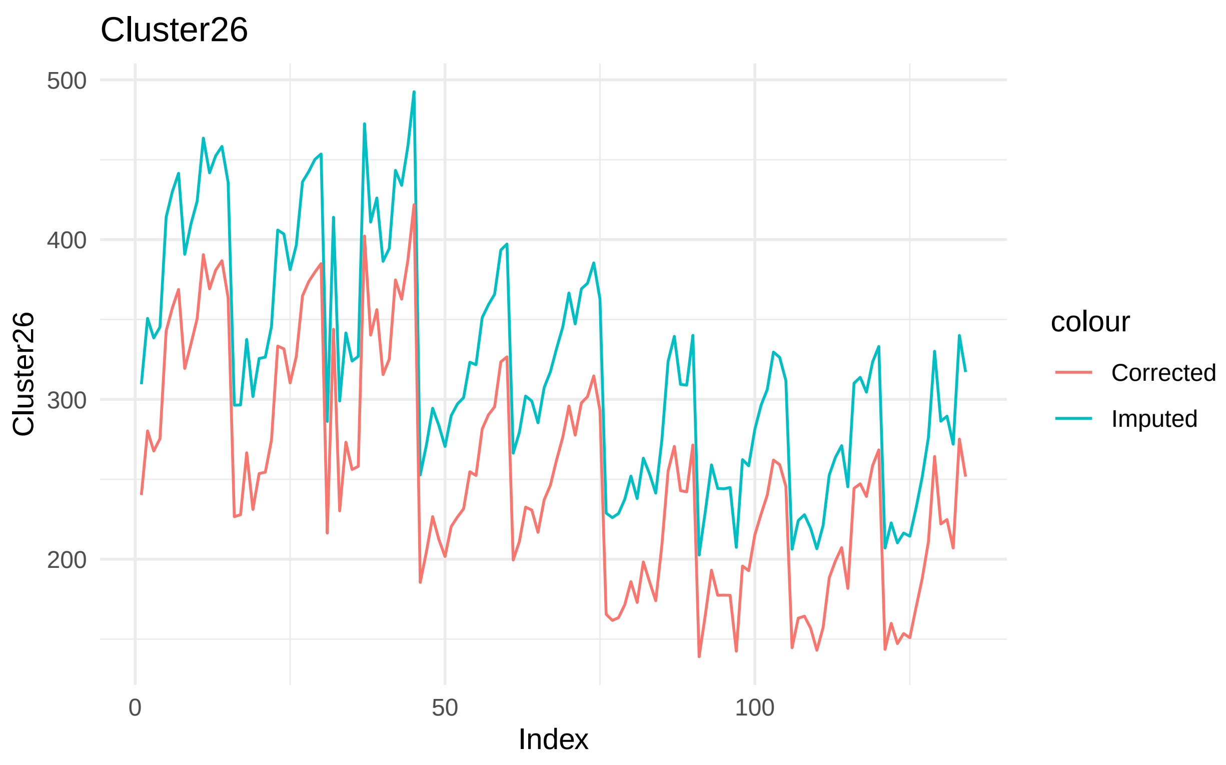

Cluster16
1000
900
800
700
600
500
Cluster16
0
50
100
Index
colour
Corrected
Imputed

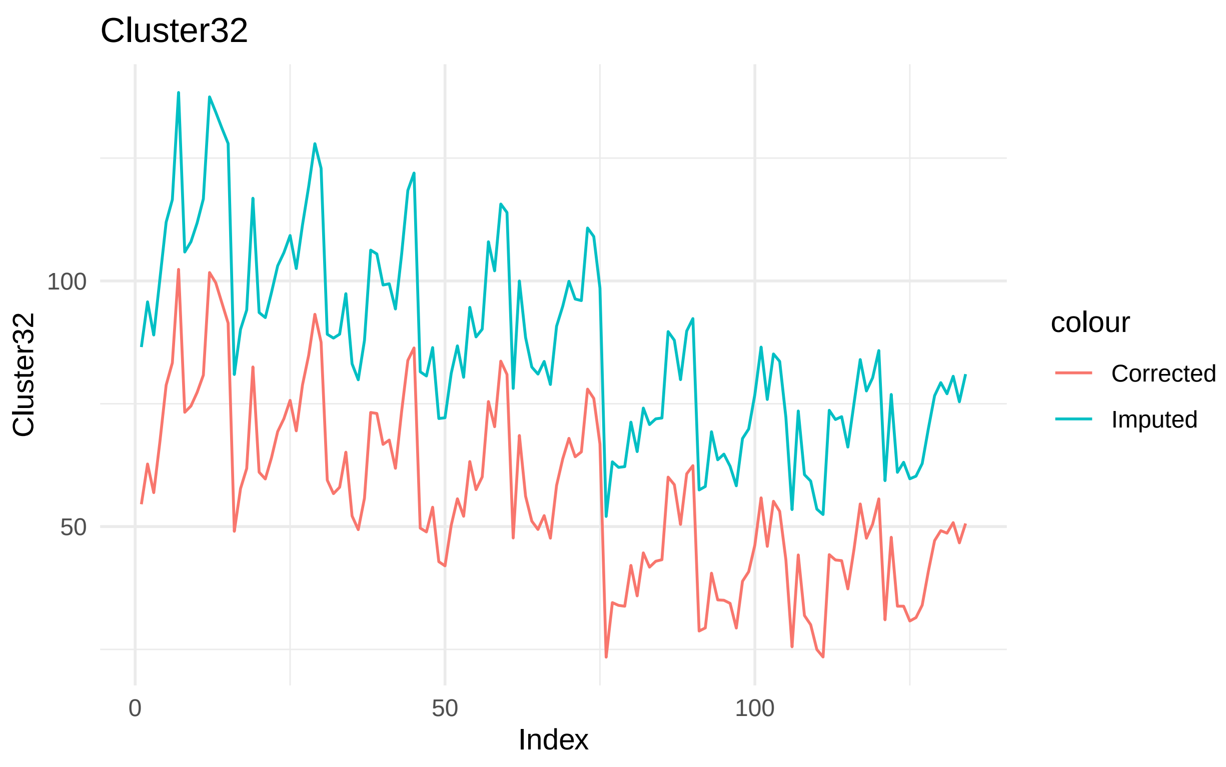

Cluster46
800
600
400
200
Cluster46
0
50
100
Index
colour
Corrected
Imputed

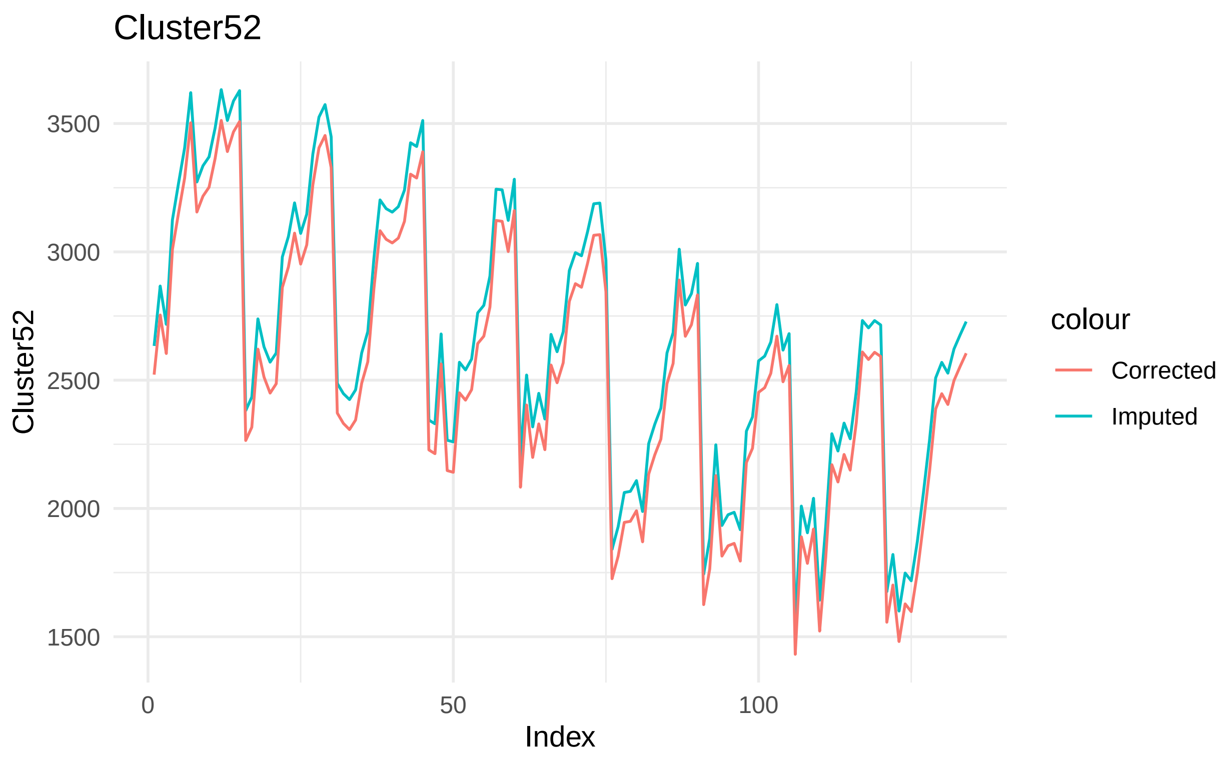

Cluster21
400
300
200
Cluster21
0
50
100
Index
colour
Corrected
Imputed

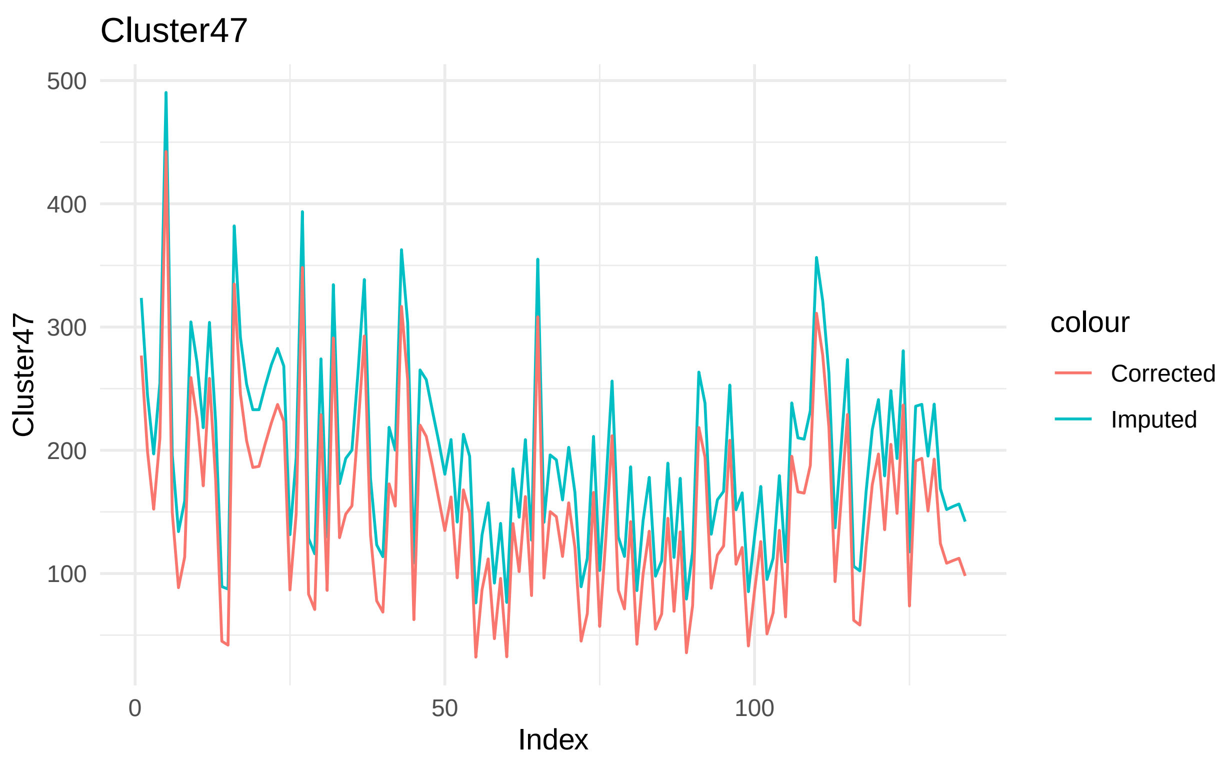

Cluster7
80
60
40
20
Cluster7
0
50
100
Index
colour
Corrected
Imputed

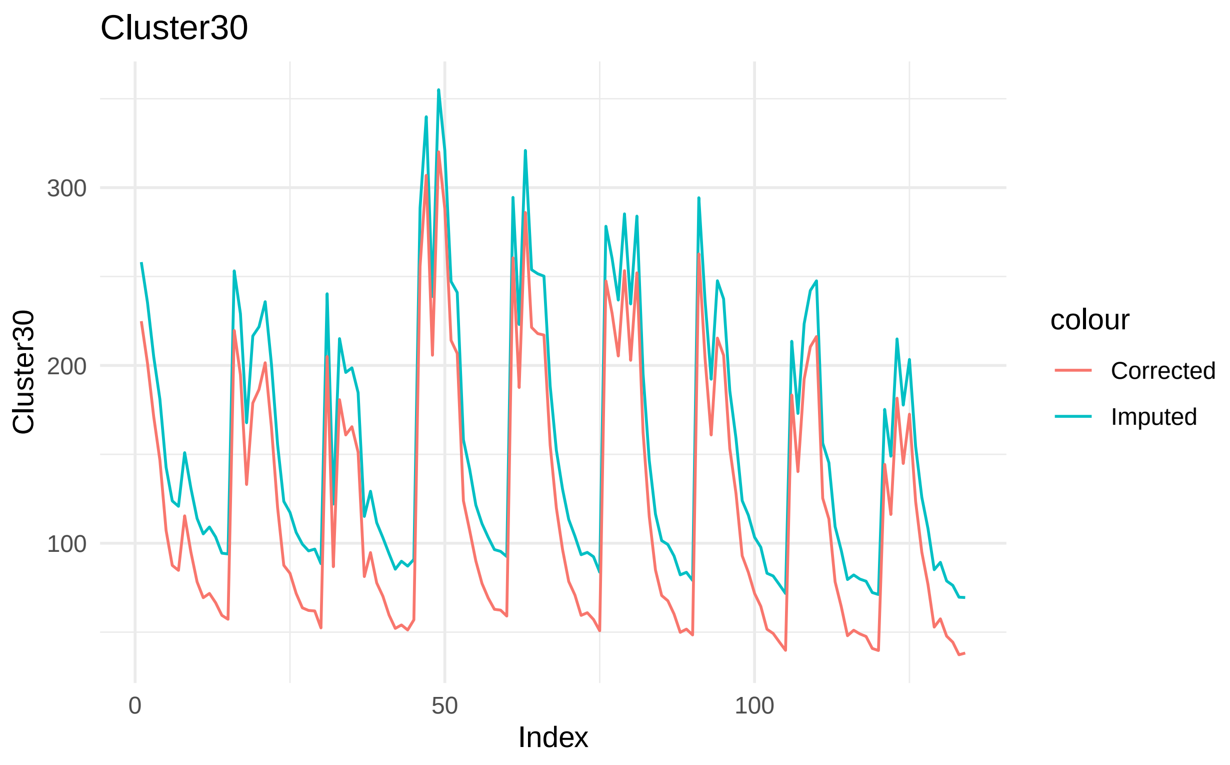

Cluster19
120
90
60
30
0
50
100
Index
Cluster19
colour
Corrected
Imputed

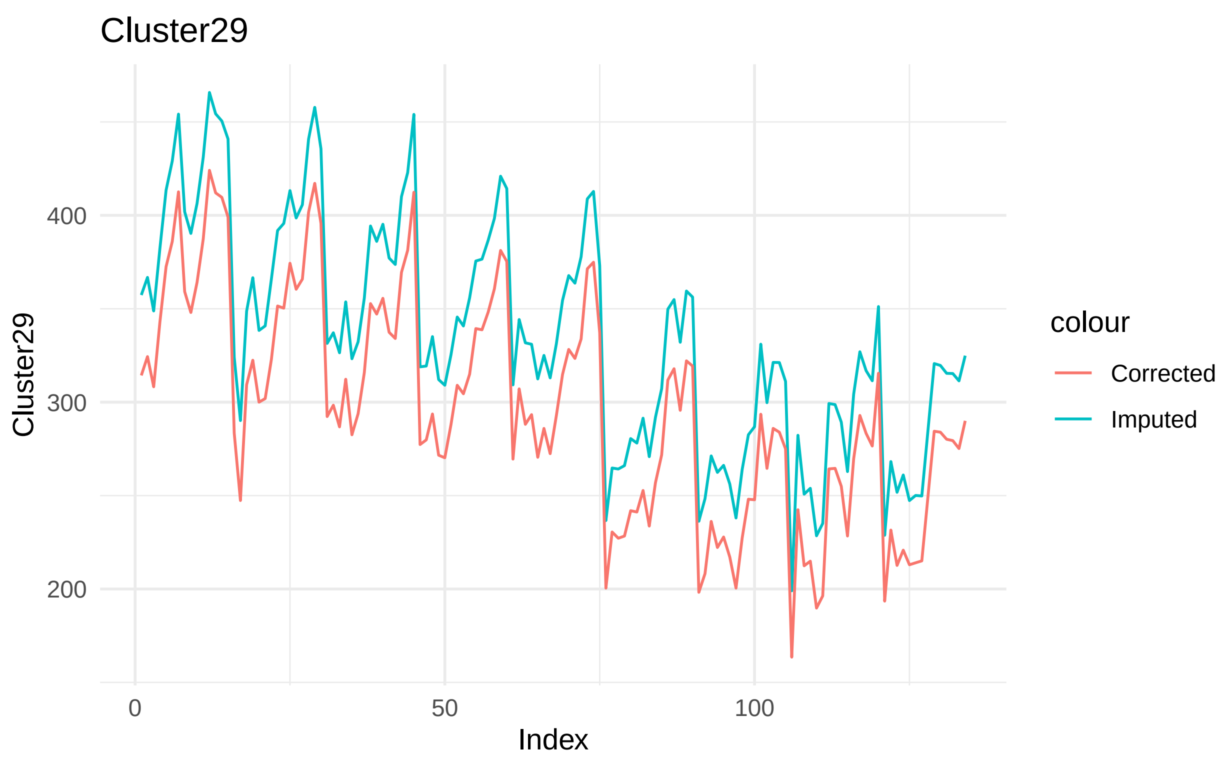

Cluster26
500
400
300
200
0
50
100
Index
Cluster26
colour
Corrected
Imputed

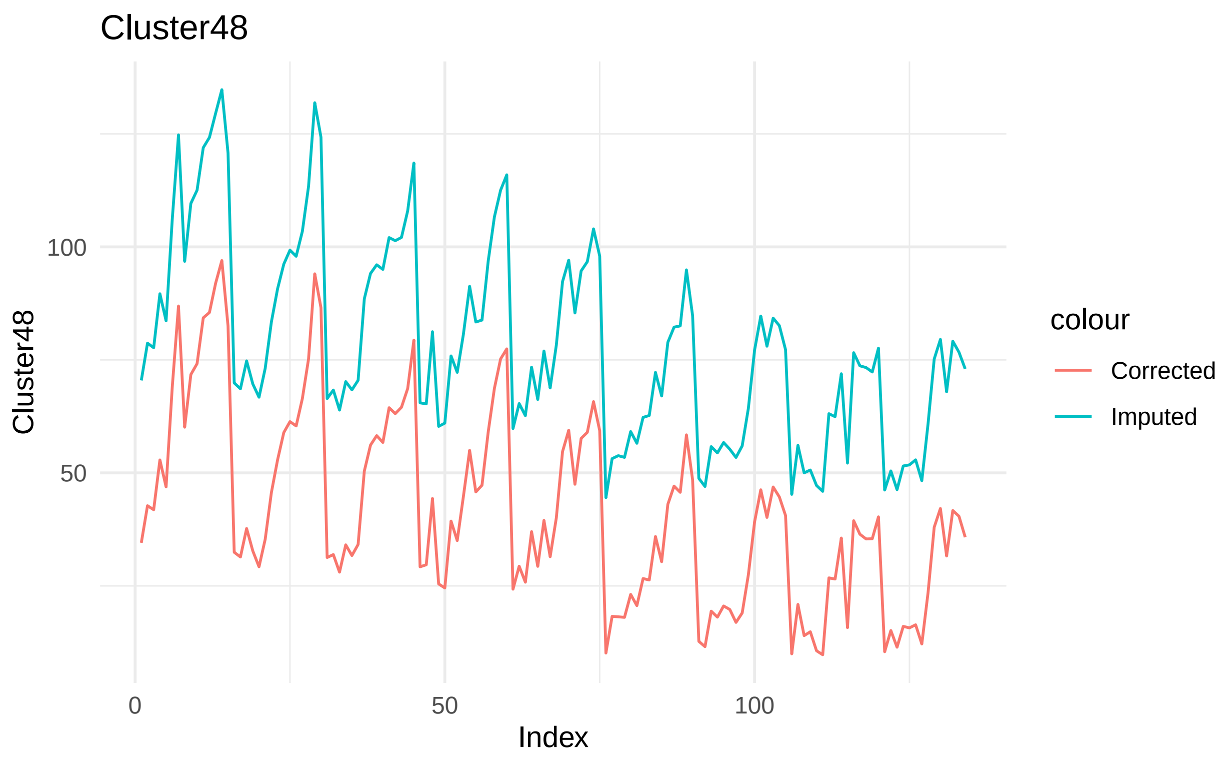

Cluster32
Cluster32
100
50
0
50
100
Index
colour
Corrected
Imputed

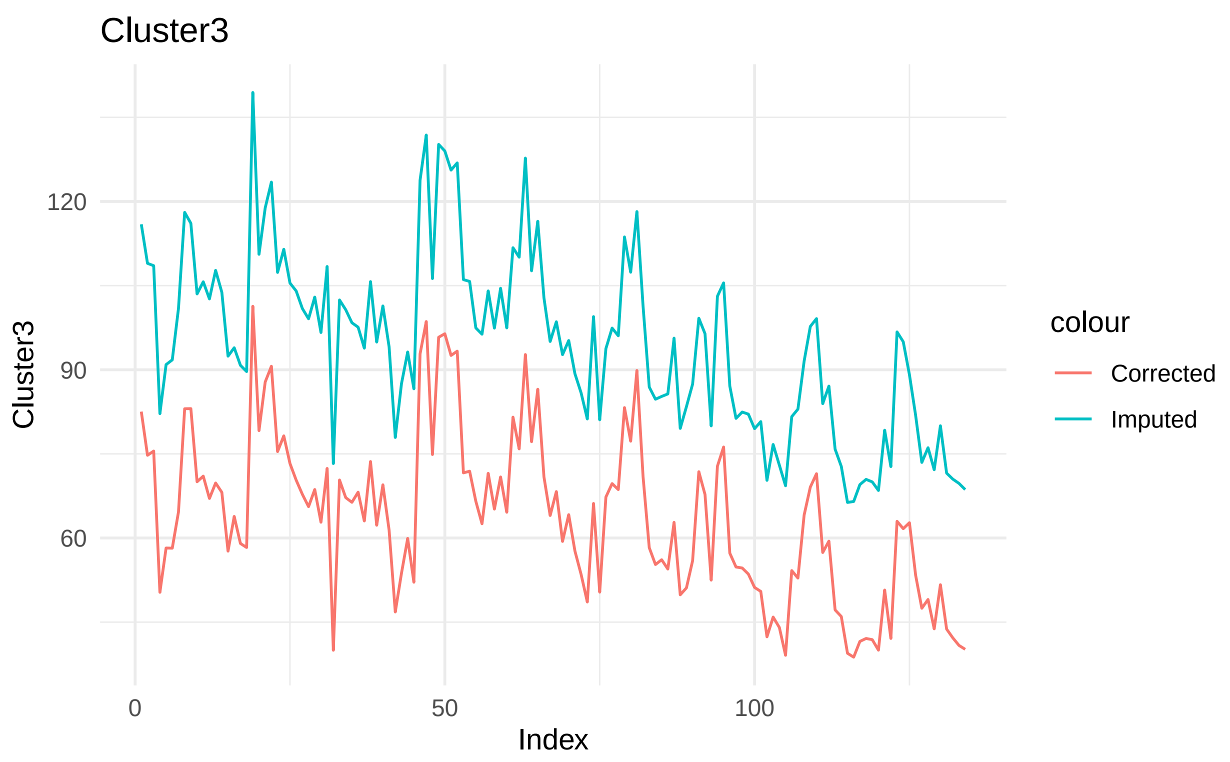

Cluster52
Cluster52
3500
3000
2500
2000
1500
0
50
100
Index
colour
Corrected
Imputed

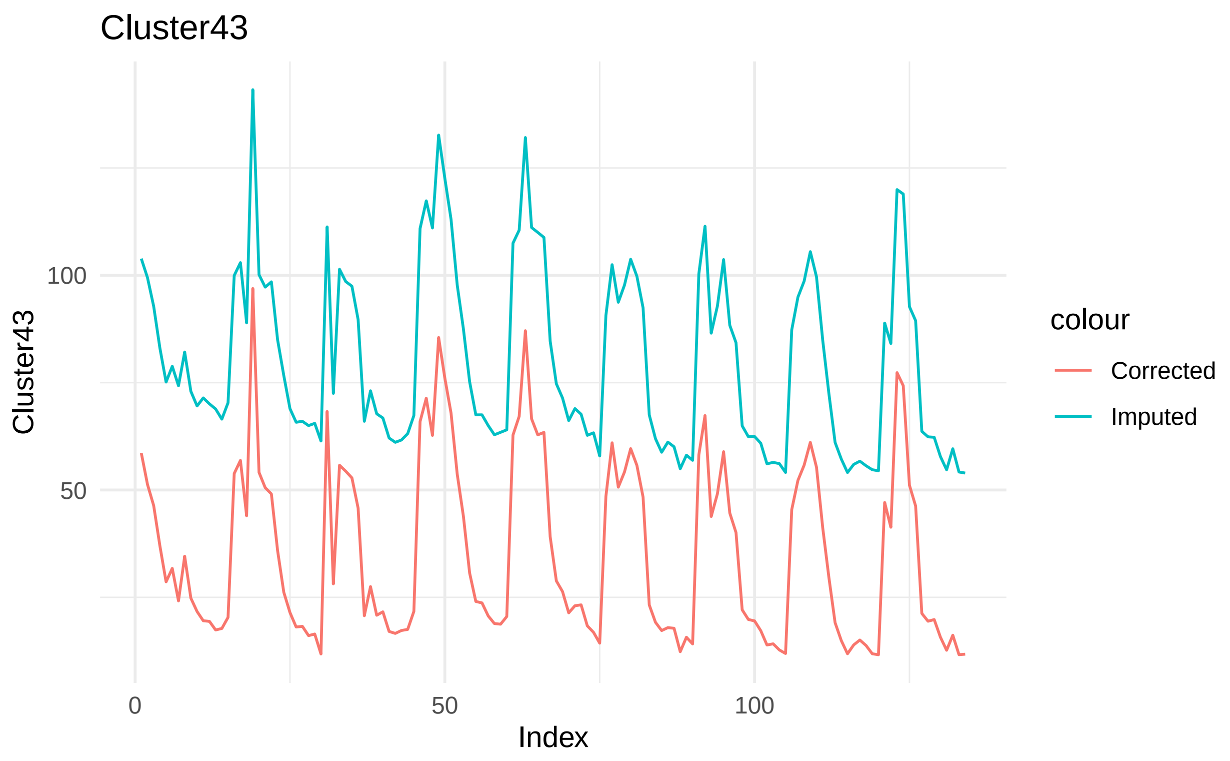

Cluster47
500
400
300
200
100
Cluster47
0
50
100
Index
colour
Corrected
Imputed

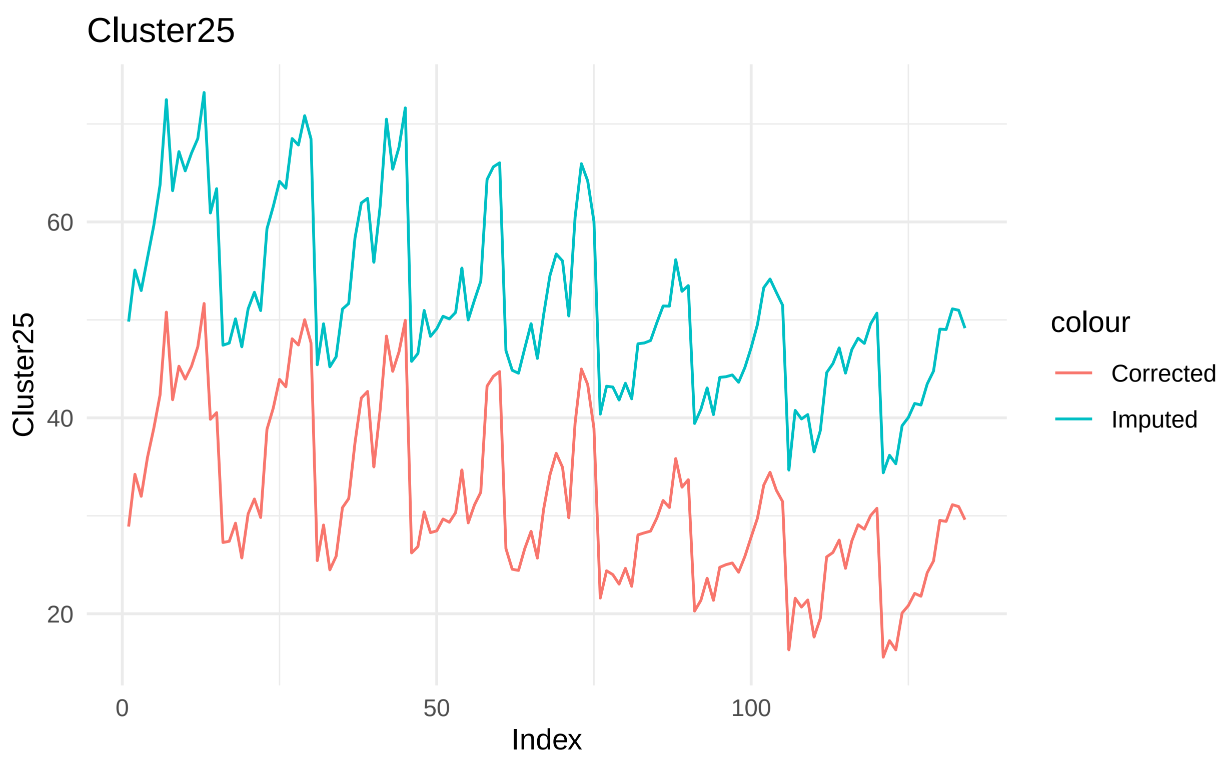

Cluster30
300
200
100
Cluster30
0
50
100
Index
colour
Corrected
Imputed

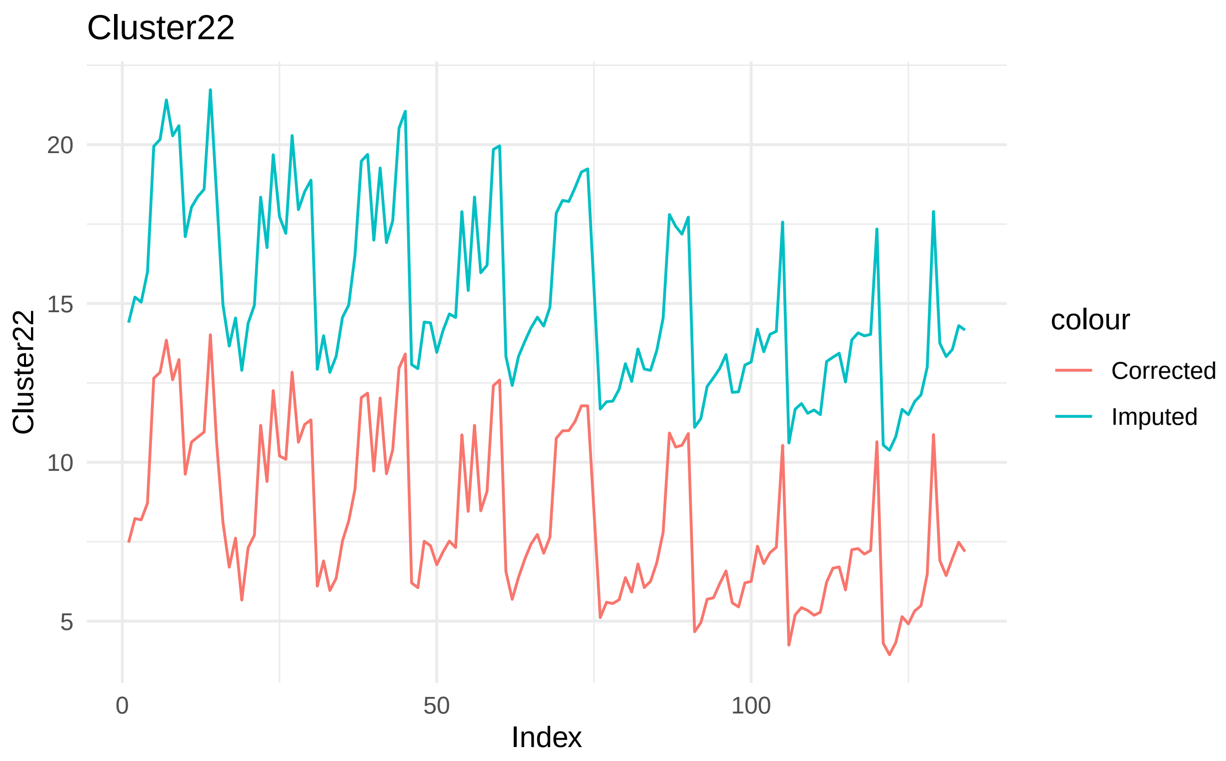

Cluster29
Cluster29
400
300
200
0
50
100
Index
colour
Corrected
Imputed

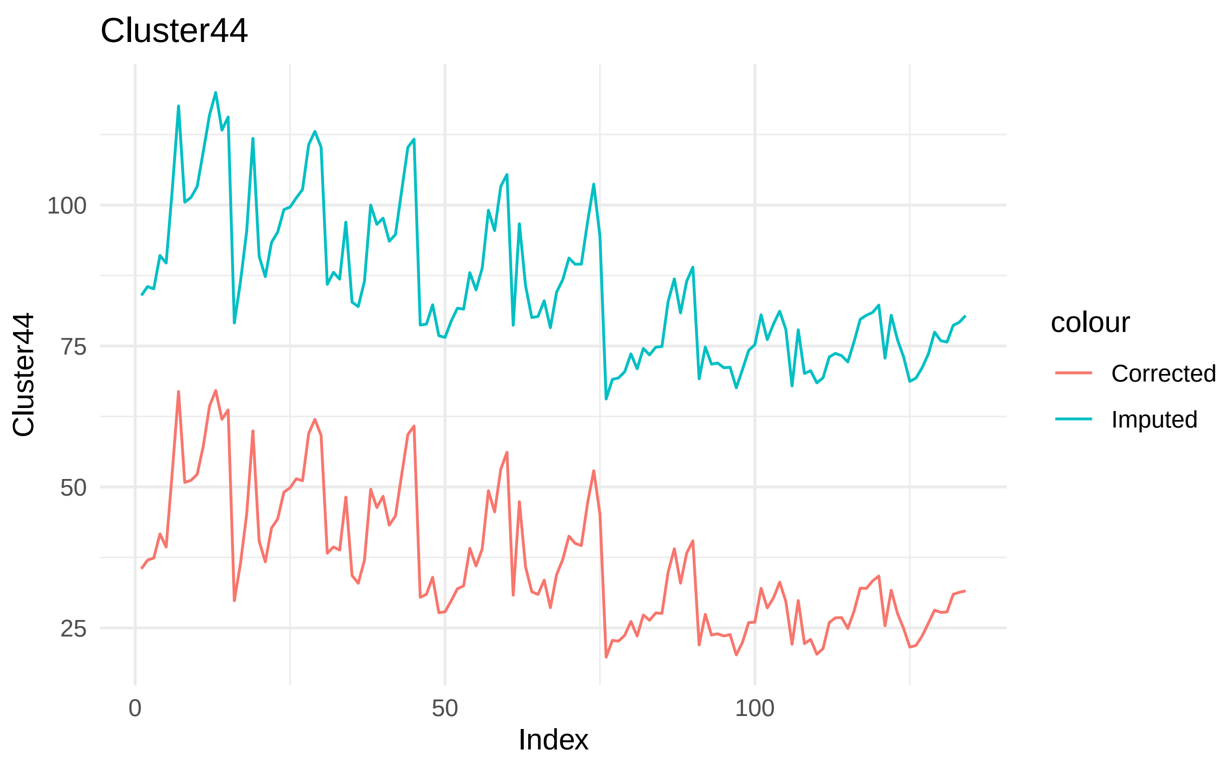

Cluster48
Cluster48
100
50
0
50
100
Index
colour
Corrected
Imputed

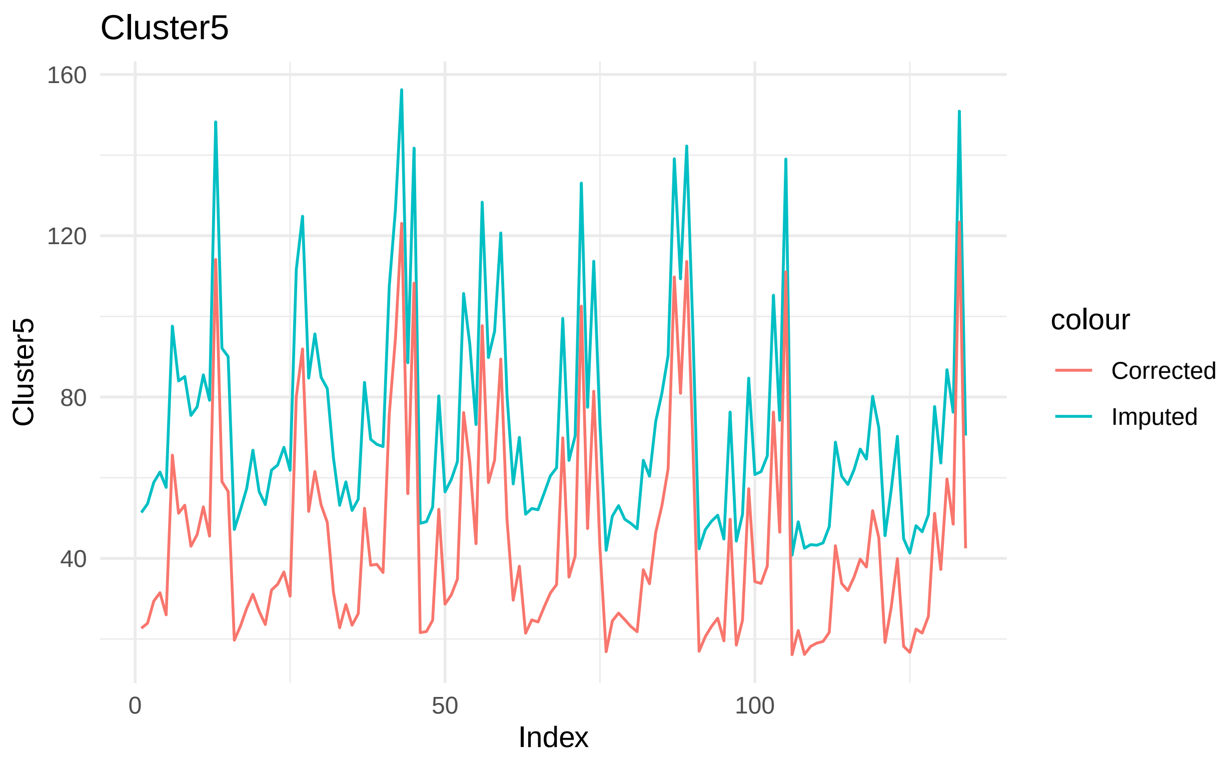

Cluster3
120
90
60
0
50
100
Index
Cluster3
colour
Corrected
Imputed

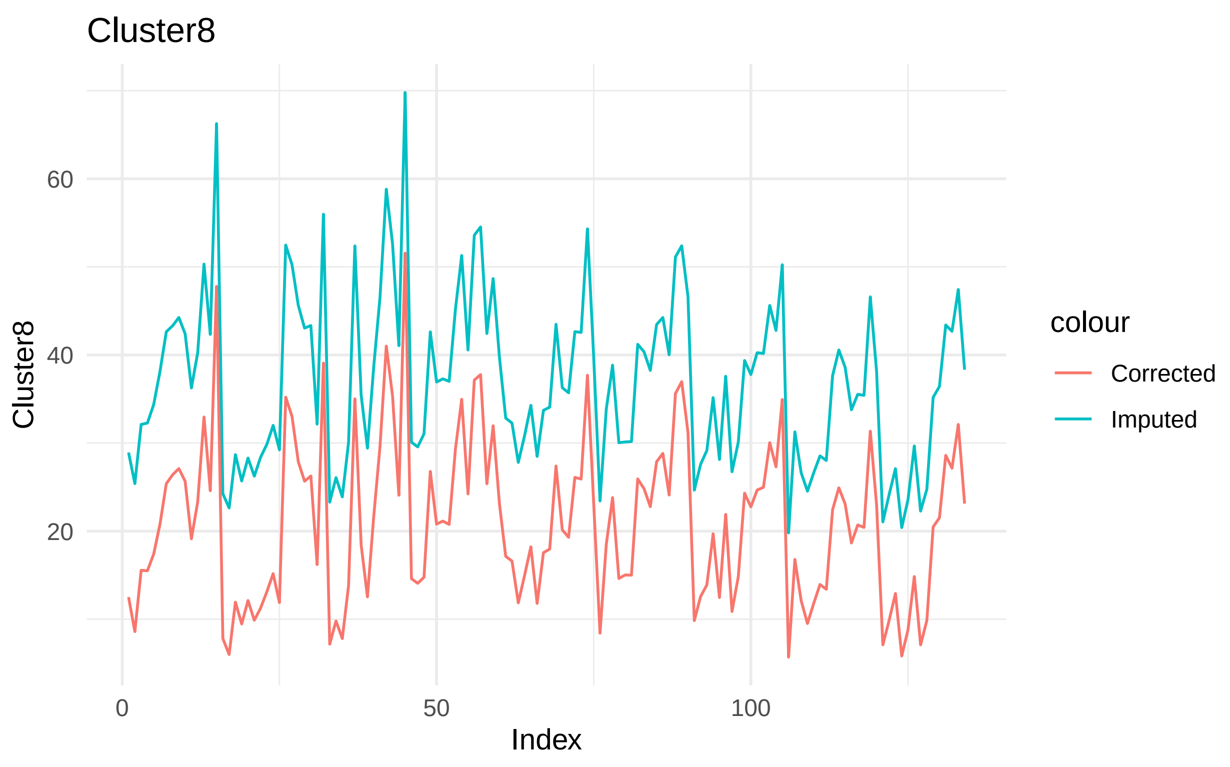

Cluster43
100
50
0
50
100
Index
Cluster43
colour
Corrected
Imputed

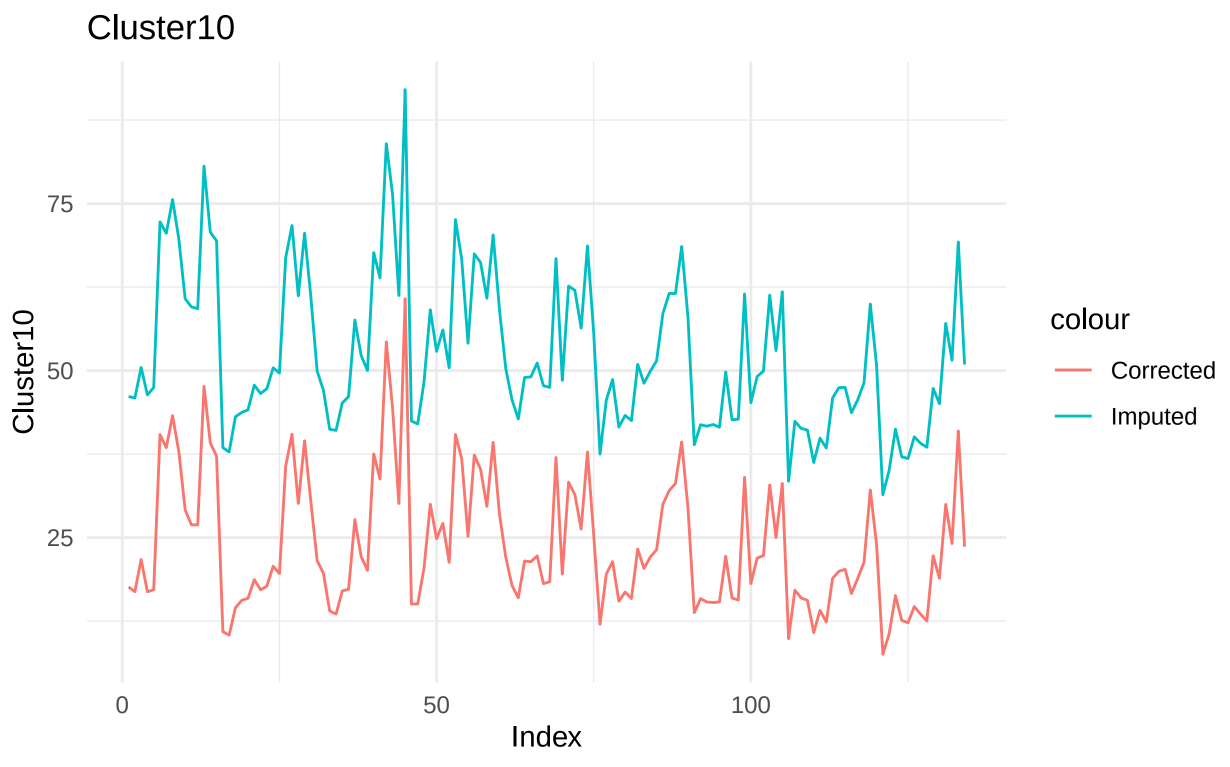

Cluster25
Cluster25
60
40
20
0
50
100
Index
colour
Corrected
Imputed

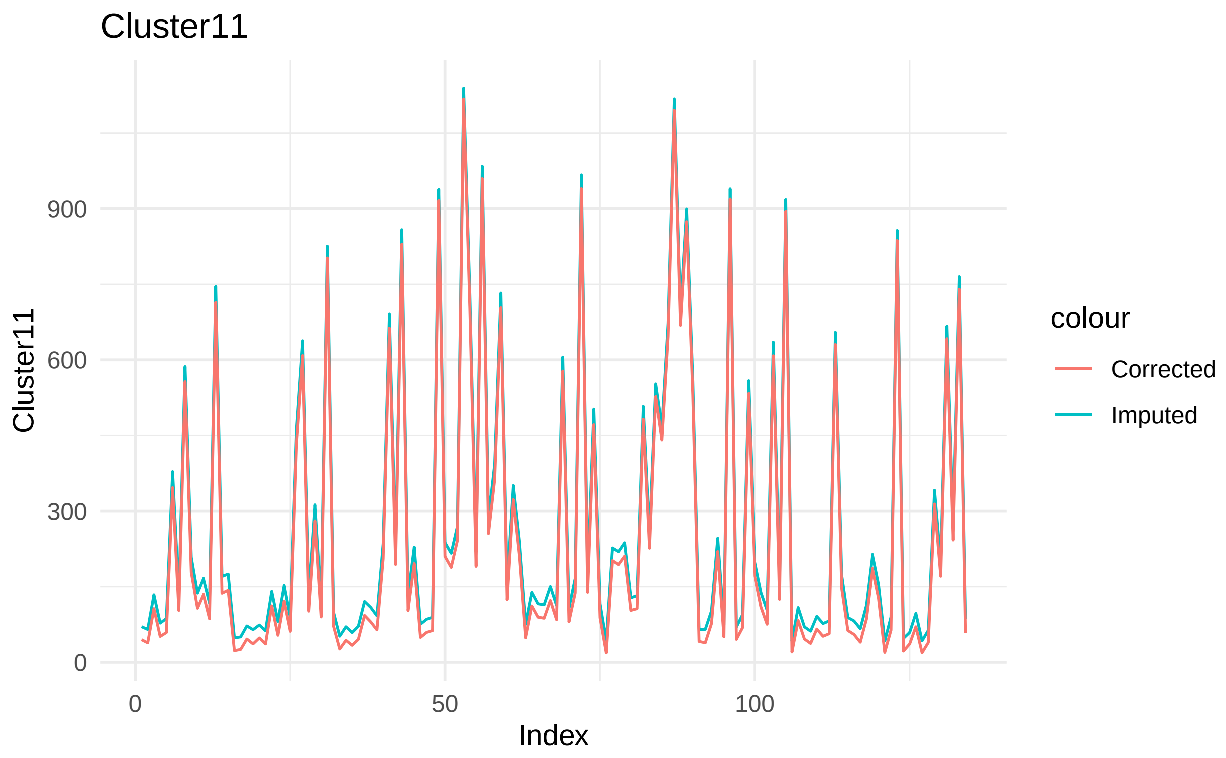

Cluster22
Cluster22
20
15
10
5
0
50
100
Index
colour
Corrected
Imputed


Cluster44
Cluster44
100
75
50
25
0
50
100
Index
colour
Corrected
Imputed


Cluster5
Cluster5
160
120
80
40
0
50
100
Index
colour
Corrected
Imputed


Cluster8
60
40
20
Cluster8
0
50
100
Index
colour
Corrected
Imputed


Cluster10
75
50
25
Cluster10
0
50
100
Index
colour
Corrected
Imputed


Cluster11
Cluster11
900
600
300
0
0
50
100
Index
colour
Corrected
Imputed