Profil_4cer_preprocessing

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4/2/2022

```
#import raw ms peaks from MZmine step 12 export
data_raw_peaks <- vroom::vroom(here::here("data-raw/0033_profil_4cer_export_040222.csv"))
```

```
## New names:
## Rows: 1942 Columns: 948
## -- Column specification
## -------------------------------------------------------- Delimiter: ";" dbl
## (946): row ID, row m/z, row retention time, 0033_LIP1p_20170412_006_CALI... lgl
## (2): row identity, ...948
## i Use `spec()` to retrieve the full column specification for this data. i
## Specify the column types or set `show_col_types = FALSE` to quiet this message.
## * `` -> `...948`
```

```
# #View data to check if it is correctly loaded
# View(data_raw_peaks)
```

```
#Select peaks based on specific IDs
#input peak ID based on viewed chromatograms
ID_list <- c("Target_17_H_ISTD" = 9,
                 "Target_17_H2O_ISTD" = 5,
                 "Target_16_H" = 1207,
                 "Target_16_H2O" = 471,
                 "Target_18_H" = 1079,
                 "Target_18_H2O" = 1022,
                 "Target_20_H" = 1049,
                 "Target_20_H2O" = 1000,
                 "Target_22_H" = 964,
                 "Target_22_H2O" = 714,
                 "Target_24_0_H" = 328,
                 "Target_24_0_H2O" = 229,
                 "Target_24_1_H" = 959,
                 "Target_24_1_H2O" = 954)

ID_list <- ID_list[order(ID_list)]

data <- data_raw_peaks %>%
    filter(data_raw_peaks$`row ID` %in% ID_list) %>%
    arrange(`row ID`) %>%
    mutate(`row identity` = names(ID_list)) %>%
    arrange(`row identity`)
```

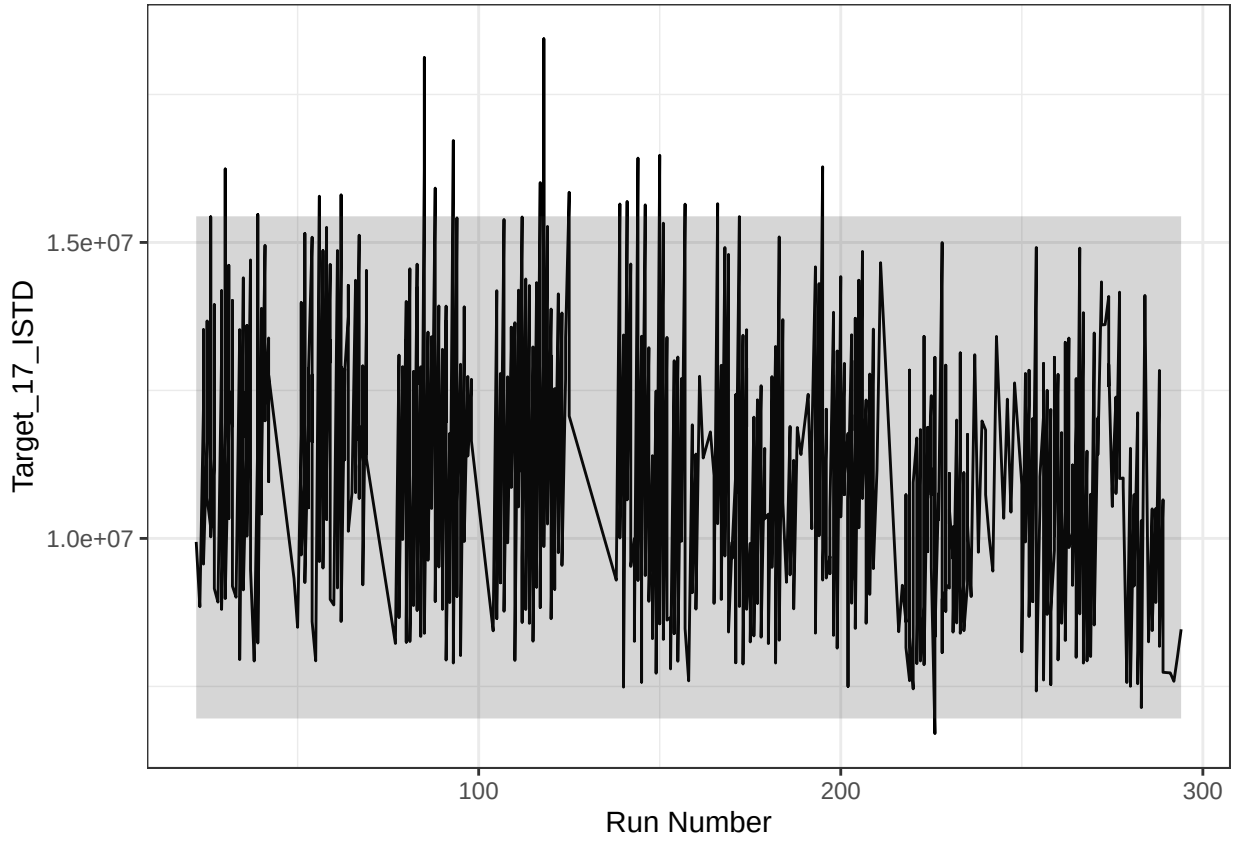
```r
rm(ID_list, data_raw_peaks)
```

```r
#NOTE This is project specific cleaning

#Remove weird artifact at the final data column
data <- data[,-length(data)]

#Keep only H2o adducts, remove RT, mz, row ID a and pivot table
data <- data %>%
    filter(grepl("H2O", `row identity`)) %>%
    mutate(ID = gsub("_H2O", "", `row identity`)) %>%
    select(-c("row m/z", "row retention time", "row identity", "row ID")) %>%
    pivot_longer(cols = -ID, names_to = "Steno ID") %>%
    pivot_wider(names_from = ID, values_from = value)


#Separate Steno ID into a new columns
data <- data %>%
    separate(`Steno ID`,
        c(  "Project_nr",
            "Method",
            "Date",
            "Run_nr",
            "Sample_ID",
            "Repeat_A",
            "Repeat_B"))
```

```
## Warning: Expected 7 pieces. Additional pieces discarded in 943 rows [1, 2, 3, 4,
## 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, ...].
```

```r
#Run plot for
Run_nr_plot <- function(Data, Target, Filter_out = FALSE) {
    Target_pos <- which(colnames(Data) %in% Target)
    Target <- sym(Target)

    tmp_bounds <- data.frame("Mean" = NA, "SD" = NA, "lower" = NA, "upper" = NA)

    Data %>%
        filter(!grepl(Filter_out, `Sample_ID`)) %>%
        pull(Target) %>%
        mean() -> tmp_bounds$Mean

    Data %>%
        filter(!grepl(Filter_out, `Sample_ID`)) %>%
        pull(Target) %>%
        sd() -> tmp_bounds$SD

    tmp_bounds$lower <- tmp_bounds$Mean - 2*tmp_bounds$SD
    tmp_bounds$upper <- tmp_bounds$Mean + 2*tmp_bounds$SD

    p <- Data %>%
        filter(!grepl(Filter_out, `Sample_ID`)) %>%
```

```
        ggplot(aes(x = as.numeric(Run_nr), y = !!Target)) +
        geom_line() +
        geom_ribbon(aes(ymin = tmp_bounds$lower, ymax = tmp_bounds$upper),
                    alpha = 0.2) +
        xlab(label = "Run Number")+
    theme_bw()

    return(p)
}

#ISTD Run nr plot
Run_nr_plot(Data = data, Target = "Target_17_ISTD", Filter_out = "^[A-Za-z]+")
```




```
#Relative Standard deviation (RSD) of Pooled samples before proxy conc. normalization
data %>%
    filter(Sample_ID == "PO") %>%
    summarise(across(starts_with("Target_"), ~ sd(.)/mean(.)*100, .names = "RSD_{.col}"))
```

```
## # A tibble: 1 x 7
##   RSD_Target_16 RSD_Target_17_ISTD RSD_Target_18 RSD_T~1 RSD_T~2 RSD_T~3 RSD_T~4
##           <dbl>              <dbl>         <dbl>   <dbl>   <dbl>   <dbl>   <dbl>
## 1          17.5               17.5          27.9    30.0    32.7    31.6    31.1
## # ... with abbreviated variable names 1: RSD_Target_20, 2: RSD_Target_22,
## #   3: RSD_Target_24_0, 4: RSD_Target_24_1
```

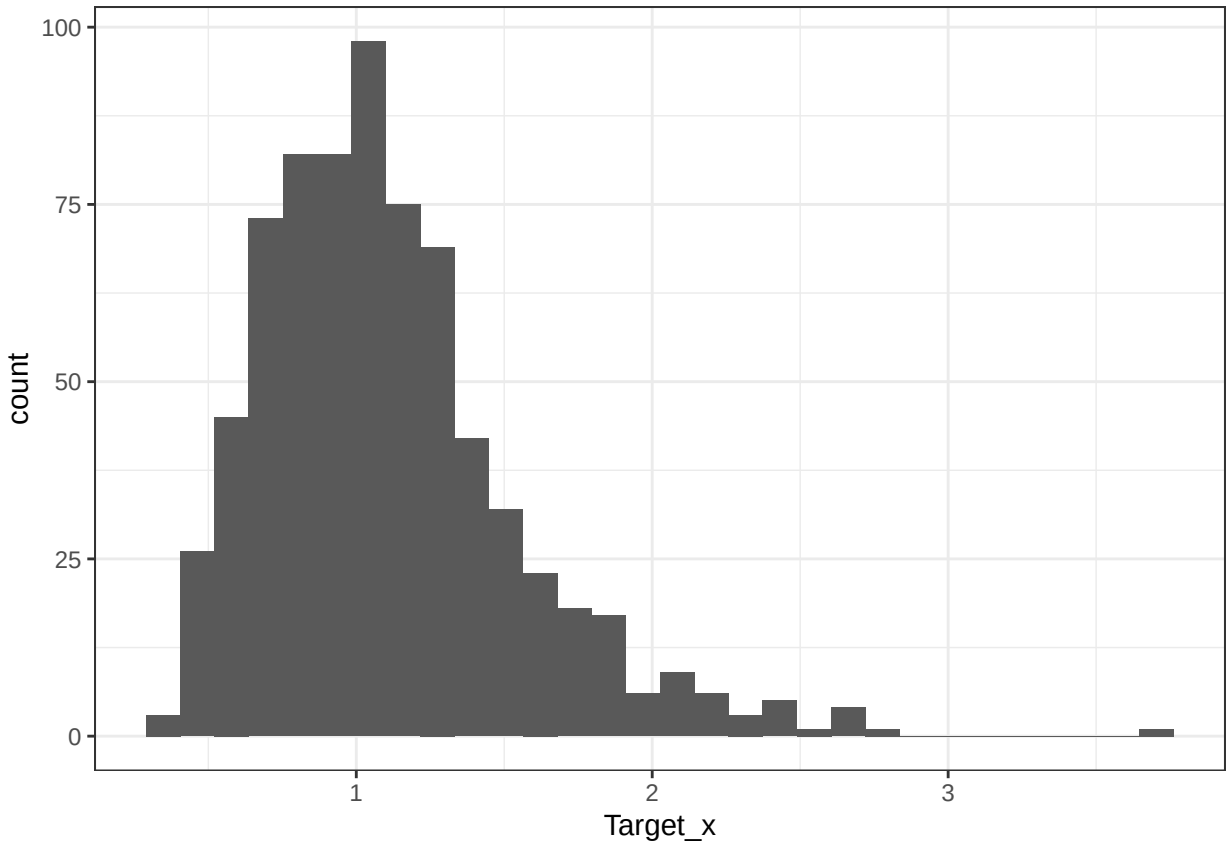
```r
#Proxy conc.
#ISTD concentration in each sample ends up at 2ug/ml
#0.01ug ISTD injected
#0.005ml injection volume
#14 is the dilution factor
data <- data %>%
    mutate(across(.cols = starts_with("Target") & !contains("ISTD"),
                  ~ 14*(((.*0.01)/Target_17_ISTD)/0.005)))

#Relative Standard deviation (RSD) of Pooled samples after proxy conc. normalization
data %>%
    filter(Sample_ID == "PO") %>%
    summarise(across(starts_with("Target_"), ~ sd(.)/mean(.)*100, .names = "RSD_{.col}"))
```

```
## # A tibble: 1 x 7
##   RSD_Target_16 RSD_Target_17_ISTD RSD_Target_18 RSD_T~1 RSD_T~2 RSD_T~3 RSD_T~4
##           <dbl>              <dbl>         <dbl>   <dbl>   <dbl>   <dbl>   <dbl>
## 1          11.2               17.5          15.1    18.5    21.8    21.3    20.9
## # ... with abbreviated variable names 1: RSD_Target_20, 2: RSD_Target_22,
## #   3: RSD_Target_24_0, 4: RSD_Target_24_1
```

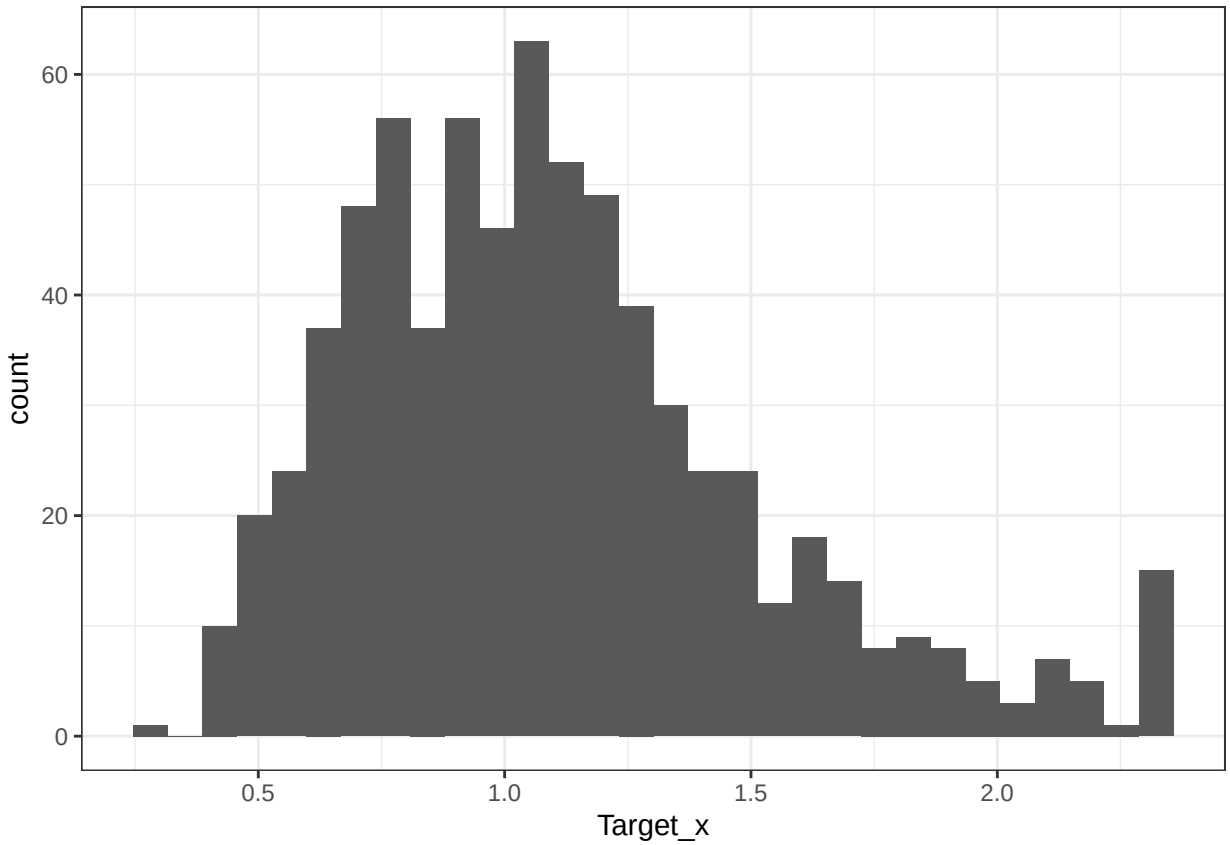
```r
#Remove QC samples and unnecessary features
data <- data %>%
    filter(!grepl("^[A-Za-z]+", `Sample_ID`)) %>%
    select(-c(Project_nr, Method, Date, Run_nr, Repeat_A, Repeat_B,)) %>%
    select(-Target_17_ISTD)
```

```r
#Ratios of interest (16:0)/(24:0), (18:0)/(24:0), (24:1)/(24:0)

#Calculate ratio of all targets against cer(24:0)
data_ratios <- data %>%
  mutate(across(contains("Target") & !contains("_24_0"),
                ~ . / Target_24_0)) %>%
  select(-Target_24_0) %>%
  rename(`Ratio 16/24:0` = Target_16) %>%
  rename(`Ratio 18/24:0` = Target_18) %>%
  rename(`Ratio 20/24:0` = Target_20) %>%
  rename(`Ratio 22/24:0` = Target_22) %>%
  rename(`Ratio 24:1/24:0` = Target_24_1)

data <- data %>%
  left_join(x = ., y = data_ratios, by = "Sample_ID")

rm(data_ratios)
```

```r
#plot distribution
data %>%
    mutate(Target_x = Target_24_1 ) %>%
    ggplot(aes(x = Target_x)) +
    geom_histogram(bins = 30) +
    theme_bw()
```




```
#Truncate outliers (outside median +- 3*sd) to median +- 3*sd
data <- data %>%
  mutate(across(starts_with("Target") | starts_with("Ratio"),
  ~ ifelse(. > median(.)+3*sd(.), median(.)+3*sd(.), .))) %>%
  mutate(across(starts_with("Target") | starts_with("Ratio"),
  ~ ifelse(. < median(.)-3*sd(.), median(.)-3*sd(.), .)))

#plot distribution
data %>%
    mutate(Target_x = Target_24_1 ) %>%
    ggplot(aes(x = Target_x)) +
    geom_histogram(bins = 30) +
    theme_bw()
```




```
#Import a curated set of the clinical variables - 667 observations
data_raw_clinical_curated <-
  vroom::vroom(file = here::here("data-raw/profil_selected_clinical_220322.csv")) %>%
  mutate(Curated = 1)
```

```
## New names:
## Rows: 667 Columns: 63
## -- Column specification
## -------------------------------------------------------- Delimiter: "," dbl
## (61): ...1, cpr, id_profil, Age, Duration_DM, Gender, Smoking, Weight, ... date
## (2): pro_date_index, pro_date_end
## i Use `spec()` to retrieve the full column specification for this data. i
## Specify the column types or set `show_col_types = FALSE` to quiet this message.
## * `` -> `...1`
```

```
#Import a non-curated set of the clinical variables - 727 observations
data_raw_clinical_all <-
  vroom::vroom(file = here::here("data-raw/PROFIL--Clinical_Data--All--201112.csv"),
    col_select = c(1:252)[!c(1:252) %in% c(241, 242, 244, 245, 402)]) %>%
  mutate(Curated = 0)
```

```
## Warning: One or more parsing issues, see `problems()` for details
```

```
## Rows: 727 Columns: 248
## -- Column specification --------------------------------------------------------
```

```
## Delimiter: ","
## dbl  (200): corenr, visit_date, age_baseline, eGFRdecline_estimate, sex, wei...
## lgl    (8): Date_FU_15, d_ckd_dod_profil, d_ckd5_profil, d_ckd5, d_ckd5_afte...
## date  (40): FU_date_death_15, FU_date_ESRD_15, FU_combined_15, DATE, Diabete...
##
## i Use `spec()` to retrieve the full column specification for this data.
## i Specify the column types or set `show_col_types = FALSE` to quiet this message.
```

```r
#NOTE col_select is used here to avoid the insane column names of the clinical data file, column nr. 24

#Create a data set from clinical_all with the observations missing from clinical_curated.
#Remove variables not included in clinical_curated as well as timing variable which are wrong.
data_raw_clinical_missing <- data_raw_clinical_all %>%
  mutate(id_profil = corenr) %>%
  filter(!id_profil %in% data_raw_clinical_curated$id_profil) %>%
  select(colnames(.)[colnames(.) %in% colnames(data_raw_clinical_curated)]) %>%
  select(!starts_with("t_"))

#Merge curated and missing data
data_clinical <- data_raw_clinical_curated %>%
  bind_rows(., data_raw_clinical_missing)

#Add blood_TGA from data_raw_clinical all
data_clinical <- data_raw_clinical_all %>%
    select(corenr, Blood_TGA) %>%
    left_join(data_clinical, .,
              by = c("id_profil" = "corenr"))

#Prepare Sample_Id for merging and organize variables of interest
data_clinical<- data_clinical %>%
  mutate(Sample_ID = as.numeric(id_profil)-16000) %>%
  select(-c("...1", "cpr", "id_profil")) %>%
  relocate(Curated, .before = 1) %>%
  relocate(starts_with("t_"), .after = pro_date_end) %>%
  relocate(starts_with("censor"), .after = pro_date_end) %>%
  relocate(contains("gfrfald30_p"), .after =  "Spiron") %>%
  relocate(contains("alb_prog"), .after =  "Spiron") %>%
  relocate(contains("ESRD_profil"), .after =  "Spiron") %>%
  relocate(contains("komb_nyre_endepunkt_p"), .after =  "Spiron") %>%
  relocate(contains("cv_komb_profil"), .after =  "Spiron") %>%
  relocate(contains("doed"), .after =  "Spiron") %>%
  relocate(Blood_TGA, .after = Blood_CREAE)

#Correct Censor data
#The Surv function expect: 0=right censored (no event), 1=event at time, 2=left censored (death)
#some variables have this setup 0=event, 1=death, 2=no event/migration and needs correction
#censor_cv_komb_profil, censor_alb_prog, censor_gfrfald30_p, censor_ESRD_profil
data_clinical <- data_clinical %>%
  mutate(across(
    .cols = c(censor_cv_komb_profil, censor_alb_prog, censor_gfrfald30_p, censor_ESRD_profil),
    ~ . + 1)) %>%
  mutate(across(
    .cols = c(censor_cv_komb_profil, censor_alb_prog, censor_gfrfald30_p, censor_ESRD_profil),
    ~ ifelse(. == 3, 0, .)))
```

```r
#The Surv function expect:0=no event, 1=event
#Some variables are recorded opposite and needs to be corrected that is:
#censor_doed_profil, censor_komb_nyre_endepunkt_p
data_clinical <- data_clinical %>%
  mutate(across(
    .cols = c(censor_doed_profil, censor_komb_nyre_endepunkt_p),
    ~ ifelse(. == 0, 1, 0)))


rm(data_raw_clinical_curated, data_raw_clinical_all, data_raw_clinical_missing)
```

```r
#Merge clinical data and peak data
data <- data %>%
    mutate(Sample_ID = as.numeric(Sample_ID)) %>%
    left_join(., data_clinical,by = "Sample_ID")

rm(data_clinical)
```

```r
#Export data
vroom::vroom_write(data, here::here("data/0033_profil_4cer_data_preprocessed.csv"))
```