PPV Bland-Altman analysis

This document contains analysis code for the Bland-Altman analysis of PPV_{GAM} vs $\text{PPV}_{\text{Classic}}$.

```
library(tidyverse)
library(patchwork)
library(ggh4x)
```

```
PPV_df <- read_csv("data/vent_setting_study-ppv.csv") |>
  mutate(
    id_f = factor(id),
    #vent_resp_len = 60 / vent_RR,
    vent_rel_vt_f = factor(vent_rel_vt, levels = c(10, 8, 6, 4)),
    vent_RR_f = factor(vent_RR, levels = c(10, 17, 24, 31)),
    vent_setting = interaction(vent_rel_vt, vent_RR, drop = TRUE)
  ) |>
  drop_na(PPV_gam)
```

Calculate difference between 1010 and the rest.

```
PPV_1010 <- filter(PPV_df, vent_RR == 10, vent_rel_vt == 10) |>
  select(id, PPV_gam, PPV_classic)

PPV_df_1010_all <- PPV_df |>
  left_join(PPV_1010, by = "id", suffix = c("", "_1010")) |>
  group_by(id_f) |>
  mutate(vent_dist = max(vent_setting_order) - vent_setting_order) |>
  ungroup() |>
  mutate(D_PPV_gam = PPV_gam - PPV_gam_1010,
         mean_PPV_gam = (PPV_gam_1010 + PPV_gam) / 2)

PPV_df_1010 <- PPV_df_1010_all |>
  filter(!(vent_RR == 10 & vent_rel_vt == 10))


PPV_vent_setting_all <- PPV_df_1010_all |>
  group_by(vent_RR, vent_rel_vt) |>
  nest() |>
  arrange(vent_RR, vent_rel_vt)

PPV_vent_setting <- PPV_vent_setting_all |>
  filter(!(vent_RR == 10 & vent_rel_vt == 10))
```

1 Plot alternative PPV vs PPV at VT=10, RR=10

```
design_no1010 <- "
  BCDE
  FGHI
  J###
"

make_vent_facet_plot <- function(data, mapping = aes(),
                                 design, remove_labels = "none") {

    ggplot(data, mapping = mapping) +
    facet_manual(vars("VT [ml kg⁻¹]" = fct_rev(factor(vent_rel_vt)),
                      "RR [min⁻¹]" = vent_RR),
                 design = design, labeller = label_both,
                 axes = "all", remove_labels = remove_labels
    ) +
    theme_paper() +
    theme(axis.title.x = element_text(hjust = 0))
}

PPV_cor_1010 <- PPV_df_1010 |>
  group_by(vent_RR, vent_rel_vt) |>
  summarise(cor = cor(PPV_gam, PPV_gam_1010, use = 'complete.obs'),
            .groups = "drop")

ppv_plot <- make_vent_facet_plot(PPV_df_1010, aes(PPV_gam, PPV_gam_1010),
                                 design = design_no1010) +
  geom_abline(slope = 1, intercept = 0, linetype = 2, color = "grey50") +
  geom_abline(aes(slope = 10/vent_rel_vt, intercept = 0),
              linetype = 1, color = "grey50",
              data = ~filter(.x, id == 1)) +
  #geom_point(size = 0.7, color = "#999999", data = ~select(.x, -vent_RR, - vent_rel_vt)) +
  geom_point(size = 0.7) +
  #stat_smooth(method = "lm", formula = y ~ 1 + x,
  #            se = FALSE, color = accent_color) +
  labs(
    x = "PPV [%] with ventilation as specified above each panel",
    y = 'PPV [%] with VT: 10 ml kg⁻¹, RR: 10 min⁻¹'
    ) +
  coord_fixed() +
  scale_x_continuous(limits=c(0, NA)) +
  scale_y_continuous(limits=c(0, NA)) +
  geom_label(data=PPV_cor_1010, aes(label=sprintf("R² = %.2f", cor^2), color = NA),
           x=15, y=0, hjust = 1, vjust = 0, show.legend = FALSE, size = 2.5,
           color = 'grey30', label.size = 0)
```

```
save_plot("extra_PPV_gam_1010", ppv_plot, width = 16, height = 12, scale = 1)
```

```
## [1] "plots/extra_PPV_gam_1010.png" "plots/extra_PPV_gam_1010.pdf"
```

2 Bland-Altman analysis

2.1 Bland-Altman analysis functions

```
calc_ba_stat <- function(data, i) {
  avg <- mean(data[i])
  std.dev <- sd(data[i])

  ul <- avg + 1.96 * std.dev
  ll <- avg - 1.96 * std.dev

  c("bias" = avg, "loa.ll" = ll, "loa.ul" = ul, "std.dev" = std.dev)
}

calc_bootstrapped_ba_stats <- function(data) {
  b <- boot::boot(data, calc_ba_stat, R = 4000)
  est_df <- broom::tidy(b, conf.int = TRUE, conf.level = 0.95, conf.method = "bca")
  est_df |>
    rename(est = statistic) |>
    select(-c(bias, std.error)) |>
    # Pivot into one row
    pivot_wider(names_from = term, values_from = c(est, conf.low, conf.high))
}
```

```
geom_est_ci <- function(var, label = "", xmax, ci_text = TRUE, text_vjust = 0.5) {
  est <- paste0("est_", var)
  conf.low <- paste0("conf.low_", var)
  conf.high <- paste0("conf.high_", var)

  list(
    geom_rect(aes(
      xmin = 0, xmax = xmax,
      ymin = .data[[conf.low]],
      ymax = .data[[conf.high]]
      ),
      fill = "#aaaaaa", alpha = 0.5
    ),
    geom_segment(aes(y = .data[[est]],
                     yend = .data[[est]],
                     x = 0, xend = xmax), linetype = 2),
```

```
    if (ci_text) {
      geom_text(
        aes(
          label = sprintf("%s: %+.2f \n[%+.2f; %+.2f]",
                          label,
                          .data[[est]], .data[[conf.low]], .data[[conf.high]]),
          x = xmax + 0.5,
          y = .data[[est]]
        ),
        size = 2.5,
        hjust = 0,
        vjust = text_vjust,
        lineheight = 1
      )
    } else {
      geom_text(aes(label = sprintf("%s: %+.2f",
                                    label,
                                    .data[[est]]),
                    x = xmax+0.5, y = .data[[est]]),
                size = 2.1, hjust = 0, vjust = 0.5, lineheight = 1
                )
    }

  )
}
```

2.2 Plot Bland-Altman analysis $\mathbf{PPV_{GAM}}$ vs $\mathbf{PPV_{Classic}}$

```
PPV_df_BA_gam_vs_classic <- PPV_df |>
  mutate(D_PPV = PPV_gam - PPV_classic,
         mean_PPV = (PPV_gam + PPV_classic) / 2)

set.seed(1)
BA_stats_gam_vs_classic <- PPV_df_BA_gam_vs_classic |>
  group_by(vent_rel_vt, vent_RR) |>
  nest() |>
  mutate(BA = map(data, ~calc_bootstrapped_ba_stats(.x$D_PPV))) |>
  unnest(BA)


# Select only 10,10 data
BA_stats_gam_vs_classic_1010 <- BA_stats_gam_vs_classic |>
  filter(vent_rel_vt == 10, vent_RR == 10)

PPV_df_BA_gam_vs_classic_1010 <- PPV_df_BA_gam_vs_classic |>
  filter(vent_rel_vt == 10, vent_RR == 10)
```

```r
max_x_val <- max(PPV_df_BA_gam_vs_classic_1010$mean_PPV)

PPV_gam_vs_classic_scatter_plot1010 <-
  PPV_df |>
  filter(vent_rel_vt == 10, vent_RR == 10) |>
  ggplot(aes(PPV_classic, PPV_gam))+
  geom_abline(intercept = 0, slope = 1, color = "#888888") +
  geom_point(size = 0.7) +
  coord_fixed() +
  labs(x = "PPV<sub>Classic</sub> [%]",
       y = "PPV<sub>GAM</sub> [%]") +
  scale_x_continuous(limits=c(0, NA), expand = expansion(add = c(0,2))) +
  scale_y_continuous(limits=c(0, NA), expand = expansion(add = c(0,2))) +
  theme(axis.title.x = ggtext::element_markdown(hjust = 0.5),
        axis.title.y = ggtext::element_markdown(hjust = 0.5),
        plot.tag.position = c(0, 1.1))

PPV_gam_vs_classic_ba_plot1010 <- ggplot(BA_stats_gam_vs_classic_1010) +
  annotate("rect", xmin = max_x_val, xmax = Inf,
           ymin = -Inf, ymax = Inf, fill = "white", color = NA) +
  geom_est_ci("bias", label = "Bias", xmax = max_x_val, text_vjust = 0.5) +
  geom_est_ci("loa.ll", label = "LoA", xmax = max_x_val, text_vjust = 0.8) +
  geom_est_ci("loa.ul", label = "LoA", xmax = max_x_val, text_vjust = 0.2) +
  annotate("segment", y = 0, yend = 0,
           x = -Inf, xend = max_x_val, color = "#555555") +
  scale_x_continuous(breaks = seq(0, 25, by = 5), expand = expansion(add = c(0,7))) +
  stat_smooth(aes(mean_PPV, D_PPV), method = "lm", formula = y ~ 1 + x,
              size = 0.5,
              se = TRUE, color = accent_color, fill = alpha(accent_color, 0.3),
              data = PPV_df_BA_gam_vs_classic_1010) +
  geom_point(aes(mean_PPV, D_PPV), size = 0.7, color = "#222222",
             data = PPV_df_BA_gam_vs_classic_1010) +
  coord_fixed(clip = "off") +
  labs(x = "(PPV<sub>GAM</sub> + PPV<sub>Classic</sub>) / 2",
       y = "PPV<sub>GAM</sub> - PPV<sub>Classic</sub>") +
  theme(axis.title.x = ggtext::element_markdown(hjust = 0.5),
        axis.title.y = ggtext::element_markdown(hjust = 1),
        plot.tag.position = c(0, 1.1))

PPV_gam_vs_classic_plot_1010 <- PPV_gam_vs_classic_scatter_plot1010 +
  PPV_gam_vs_classic_ba_plot1010 +
  plot_annotation(tag_levels = "a")

save_plot("extra_PPV_gam_vs_classic_1010", PPV_gam_vs_classic_plot_1010,
          width = 12, height = 4, scale = 1)
```

```
## [1] "plots/extra_PPV_gam_vs_classic_1010.png"
```

```
## [2] "plots/extra_PPV_gam_vs_classic_1010.pdf"
```

Compare PPV_{GAM} and $\text{PPV}_{\text{Classic}}$ for all settings.

```
design_all <- "
  A###
  BCDE
  FGHI
  J###
"

max_x_val <- max(PPV_df_BA_gam_vs_classic$mean_PPV)

ppv_gam_vs_classic_ba_plot <- make_vent_facet_plot(BA_stats_gam_vs_classic,
                                                   design = design_all) +
  # Rect behind labels
  annotate("rect", xmin = max_x_val, xmax = Inf,
           ymin = -Inf, ymax = Inf, fill = "white", color = NA) +
  geom_est_ci("bias", label = "Bias", xmax = max_x_val, text_vjust = 0.5) +
  geom_est_ci("loa.ll", label = "LoA", xmax = max_x_val, text_vjust = 1) +
  geom_est_ci("loa.ul", label = "LoA", xmax = max_x_val, text_vjust = 0) +
  annotate("segment", y = 0, yend = 0,
           x = -Inf, xend = max_x_val, color = "#555555") +
  scale_x_continuous(breaks = seq(0, 25, by = 5), expand = expansion(add = c(0,7))) +
  scale_y_continuous(breaks = seq(-15, 5, by = 5), expand = expansion(add = c(1,0))) +
  stat_smooth(aes(mean_PPV, D_PPV), method = "lm", formula = y ~ 1 + x,
              size = 0.5,
              se = TRUE, color = accent_color, fill = alpha(accent_color, 0.3),
              data = PPV_df_BA_gam_vs_classic) +
  geom_point(aes(mean_PPV, D_PPV), size = 0.7, color = "#222222",
             data = PPV_df_BA_gam_vs_classic) +
  coord_fixed(clip = "off") +
  labs(x = "(PPV<sub>GAM</sub> + PPV<sub>Classic</sub>) / 2",
       y = "PPV<sub>GAM</sub> - PPV<sub>Classic</sub>") +
  theme(axis.title.x = ggtext::element_markdown(hjust = 0.05),
        axis.title.y = ggtext::element_markdown(hjust = 0.5))

save_plot("suppl_PPV_BA_gam_vs_classic", ppv_gam_vs_classic_ba_plot,
          width = 18, height = 12, scale = 1.5)
```

```
## [1] "plots/suppl_PPV_BA_gam_vs_classic.png"
## [2] "plots/suppl_PPV_BA_gam_vs_classic.pdf"
```

3 Plot PPV by Respiratory rate / Heart rate

```
PPV_hr_rr_df <- PPV_df_BA_gam_vs_classic |>
  filter(vent_rel_vt %in% c(6, 8))

hr_rr_common_layers <- list(
  geom_point(aes(color=fct_rev(vent_RR_f), shape=vent_rel_vt_f), size = 1),
  geom_vline(xintercept = 3.6, linetype = 2, color = "#888888"),
  labs(x = "",
       color = "Respiratory rate [min^-1]",
       shape = "Tidal volume [ml kg^-1]"),
  coord_cartesian(clip = "off"),
  scale_shape_manual(values = c(16,1, 2, 3)),
  #scale_color_brewer(palette = "Set2"), # use default color
  scale_x_continuous(breaks = c(2.5, 3.6, 5, 7.5, 10)),
  theme(
    axis.title.y = ggtext::element_markdown(),
    legend.direction = "horizontal",
    legend.box = "vertical",
    plot.tag.position = c(0, 1.1)
  )
)


classic_plot <- PPV_hr_rr_df |>
  ggplot(aes(hr_rr_ratio, PPV_classic)) +
  hr_rr_common_layers +
  labs(y = "PPV<sub>Classic</sub> [%]")


gam_plot <- PPV_hr_rr_df |>
  ggplot(aes(hr_rr_ratio, PPV_gam)) +
  hr_rr_common_layers +
  labs(y = "PPV<sub>GAM</sub> [%]")

diff_plot <- PPV_hr_rr_df |>
  ggplot(aes(hr_rr_ratio, D_PPV)) +
  geom_hline(yintercept = 0, color = "#222222", size = 0.4) +
  hr_rr_common_layers +
  labs(y = "PPV<sub>GAM</sub> - PPV<sub>Classic</sub>",
       x = "Heart rate / respiratory rate\n[beats / breath]")

comb_gam_classic_plot <- (classic_plot + gam_plot + diff_plot) +
  plot_layout(ncol = 1, guides = "collect") +
  plot_annotation(tag_levels = "a",
                  theme = theme(legend.position = "bottom",
                                legend.box = "vertical",
```

```
                                #legend.box.just = "left",
                                legend.spacing = unit(-0.8, "lines")))

save_plot("fig4_heart_rate_resp_rate", comb_gam_classic_plot,
          width = 10, height = 12, scale = 1)
```

```
## [1] "plots/fig4_heart_rate_resp_rate.png" "plots/fig4_heart_rate_resp_rate.pdf"
```

4 Table of Bland-Altman statistics for all settings

```
BA_stats_gam_vs_classic |>
  select(-data) |>
  pivot_longer(-starts_with("vent_"), names_sep = "_", names_to = c(".value", "name")) |>
  mutate(value = sprintf("%.2f [%.2f; %.2f]", est, conf.low, conf.high)) |>
  select(starts_with("vent_"), name, value) |>
  pivot_wider(names_from = name, values_from = value) |>
  knitr::kable(digits = 2, booktabs=TRUE) |>
  kableExtra::kable_styling(latex_options=c("scale_down", "HOLD_position"))
```

vent_rel_vt	vent_RR	bias	loa.ll	loa.ul	std.dev
6	31	1.18 [0.71; 1.54]	-1.73 [-3.83; -0.87]	4.09 [3.32; 5.36]	1.48 [1.09; 2.33]
8	31	1.40 [0.99; 1.86]	-1.54 [-2.55; -0.92]	4.34 [3.54; 5.67]	1.50 [1.17; 1.99]
6	24	0.52 [0.18; 0.83]	-1.86 [-2.78; -1.19]	2.90 [2.41; 3.79]	1.21 [0.94; 1.61]
8	24	0.97 [0.58; 1.32]	-1.65 [-3.01; -0.99]	3.58 [2.99; 4.48]	1.33 [1.05; 1.86]
6	17	0.12 [-0.07; 0.29]	-1.16 [-1.68; -0.84]	1.39 [1.14; 1.79]	0.65 [0.53; 0.86]
8	17	0.30 [0.05; 0.52]	-1.37 [-2.11; -0.92]	1.97 [1.64; 2.48]	0.85 [0.68; 1.14]
4	10	-0.64 [-1.17; -0.31]	-3.71 [-5.91; -2.41]	2.43 [1.65; 3.63]	1.57 [1.05; 2.42]
6	10	-0.37 [-0.66; -0.15]	-2.13 [-2.88; -1.58]	1.40 [1.13; 1.81]	0.90 [0.71; 1.18]
8	10	-0.28 [-0.56; -0.09]	-1.84 [-2.87; -1.31]	1.29 [0.96; 1.83]	0.80 [0.59; 1.21]
10	10	-0.36 [-0.75; -0.08]	-2.87 [-4.10; -1.99]	2.16 [1.67; 2.83]	1.28 [0.94; 1.73]

5 Difference between PPV_{GAM} and $PPV_{Classic}$ for high and low HR/RR ratio

```
BA_hr_rr_PPV <- PPV_hr_rr_df |>
  mutate(hr_rr_group = cut(hr_rr_ratio, breaks = c(0,3.6,Inf),
                           include.lowest = TRUE, right = FALSE)) |>
  group_by(hr_rr_group) |>
  nest() |>
  mutate(BA = map(data, ~calc_bootstrapped_ba_stats(.x$D_PPV))) |>
  unnest(BA)
```

```
BA_hr_rr_PPV |>
  select(hr_rr_group,
         est_bias, conf.low_bias, conf.high_bias,
         est_loa.ll, conf.low_loa.ll, conf.high_loa.ll,
         est_loa.ul, conf.low_loa.ul, conf.high_loa.ul
         ) |>
  pivot_longer(-hr_rr_group, names_sep = "_", names_to = c(".value", "name")) |>
  mutate(value = sprintf("%.2f [%.2f; %.2f]", est, conf.low, conf.high)) |>
  select(hr_rr_group, name, value) |>
  pivot_wider(names_from = name, values_from = value) |>
  knitr::kable(digits = 2, booktabs=TRUE) |>
  kableExtra::kable_styling(latex_options=c("scale_down", "HOLD_position"))
```

hr_rr_group	bias	loa.ll	loa.ul
[0,3.6)	0.94 [0.76; 1.12]	-1.71 [-2.29; -1.37]	3.59 [3.21; 4.08]
[3.6,Inf]	-0.09 [-0.23; 0.03]	-1.85 [-2.25; -1.55]	1.67 [1.48; 1.90]

High HR/RR

```
t.test(PPV_hr_rr_df$D_PPV[PPV_hr_rr_df$hr_rr_ratio >= 3.6])
```

```
##
##  One Sample t-test
##
## data:  PPV_hr_rr_df$D_PPV[PPV_hr_rr_df$hr_rr_ratio >= 3.6]
## t = -1.3889, df = 181, p-value = 0.1666
## alternative hypothesis: true mean is not equal to 0
## 95 percent confidence interval:
##  -0.22383405  0.03889759
## sample estimates:
##   mean of x
## -0.09246823
```

Low HR/RR

```
t.test(PPV_hr_rr_df$D_PPV[PPV_hr_rr_df$hr_rr_ratio < 3.6])
```

```
##
##  One Sample t-test
##
## data:  PPV_hr_rr_df$D_PPV[PPV_hr_rr_df$hr_rr_ratio < 3.6]
## t = 10.354, df = 220, p-value < 2.2e-16
## alternative hypothesis: true mean is not equal to 0
```

```
## 95 percent confidence interval:
##  0.7616995 1.1198177
## sample estimates:
## mean of x
## 0.9407586
```