KinfitR_vs_PMOD

Jonathan Tjerkaski

23 June 2019

Contents

Aims

The aim of this assignment is to analyze the PK11195 data in kinfitr

Libraries

CRAN libraries

package installation

```
install.packages("tidyverse")
install.packages("stringr")
install.packages("corrplot")
install.packages("grid")
install.packages("gridExtra")
install.packages("RColorBrewer")
install.packages("psych")
install.packages("readxl")
install.packages("pracma")
install.packages("lme4")
```

```
install.packages("rjags")
install.packages("knitr")
install.packages("cowplot")
install.packages("corrplot")
install.packages("viridis")
install.packages("janitor")
```

First, the libraries for the analysis and plotting are loaded.

```
library(stringr)
library(corrplot)
library(grid)
library(gridExtra)
library(RColorBrewer)
library(psych)
library(readxl)
library(pracma)
library(lme4)
library(rjags)
library(knitr)
library(cowplot)
library(corrplot)
library(viridis)
library(janitor)
library(tidyverse)
library(kableExtra)
library(corrr)
library(magick)
library(webshot)
```

Non-CRAN libraries

The libraries above can be installed from CRAN. Those which cannot are installed as follows:

```
install.packages("devtools")  # If you do not already have devtools
devtools::install_github("mathesong/kinfitr")
devtools::install_github("mathesong/granviller")
devtools::install_github("mvuorre/vmisc")
devtools::install_github("mathesong/kipettools")
devtools::install_github("mathesong/relfeas")
```

Loading Non_CRAN libraries and setting theme

```
library(kinfitr)
library(vmisc)
library(kipettools)
library(granviller)
library(relfeas)

theme_set(theme_light())
```

Macroparameters - Tables 1 and 2

Load both datasets

```
kinfitr_macro <- readRDS('Data_PMOD_RDS/kinfitr_macroparameters.rds')

pmod_macro <- readRDS('Data_PMOD_RDS/pmod_macroparameters.rds')
```

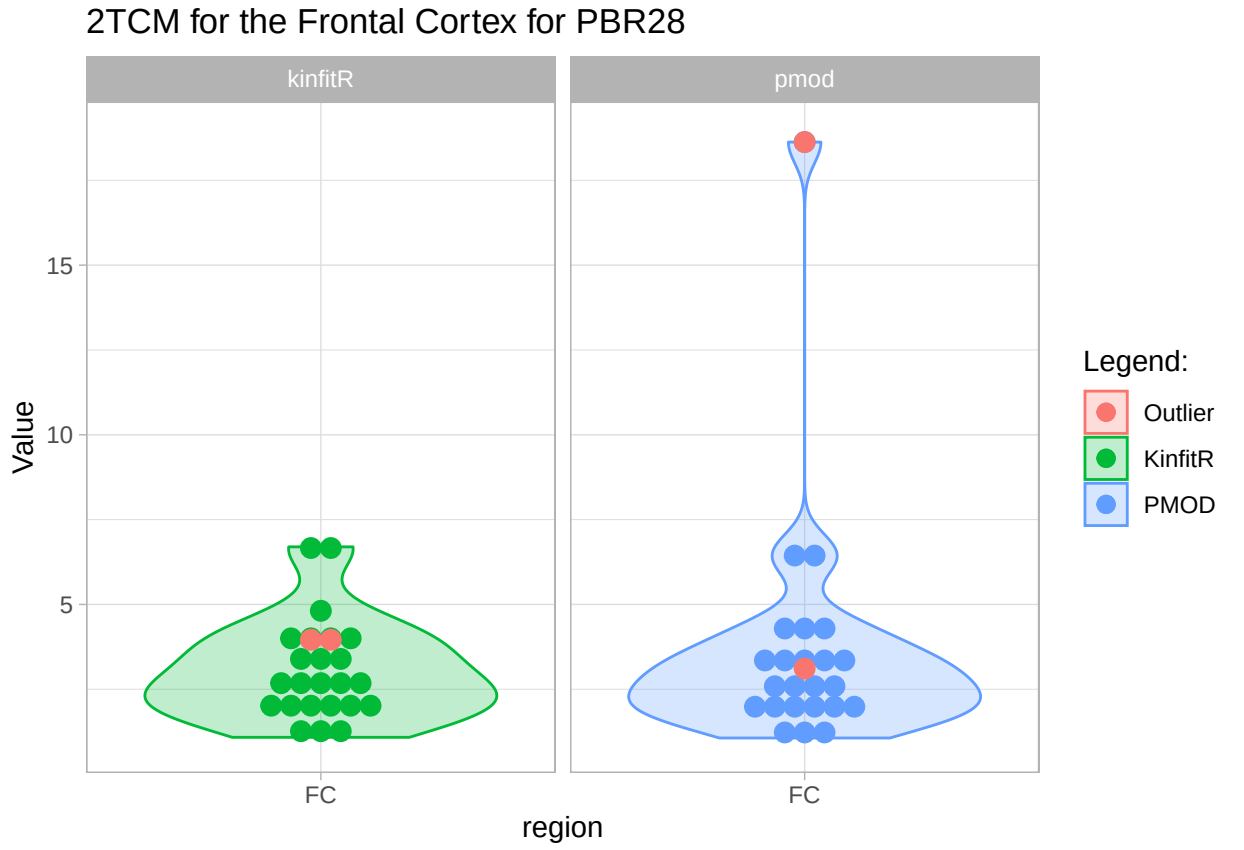
Combine datasets

```
pmod_macro <- pmod_macro %>%
  mutate(PETNo = as.numeric(PETNo))

macro <- bind_rows(kinfitr_macro, pmod_macro) %>%
  rename(Ligand = tracer, Model = model) %>%
  mutate(Model = str_replace(string = Model, pattern = "mrtm2", replacement = "MRTM2")) %>%
  mutate(Model = str_replace(string = Model, pattern = "srtm", replacement = "SRTM")) %>% mutate(Model =
  mutate(Model = str_replace(string = Model, pattern = "two_tcm", replacement = "2TCM")) %>% mutate(Mod
  mutate(Model = str_replace(string = Model, pattern = "logan", replacement = "Logan"))
```

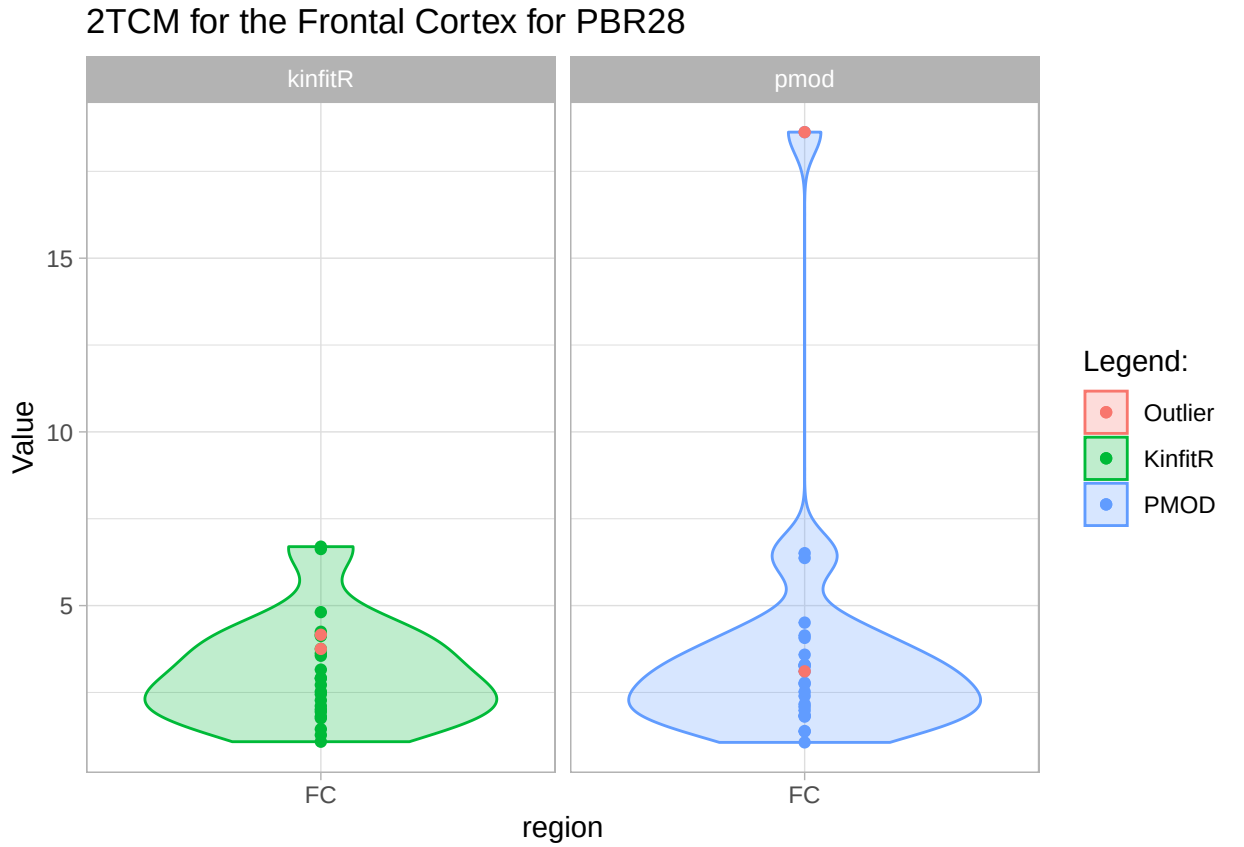
#outlier violin plots

Plots showing the outlier, which was excluded from the final analysis

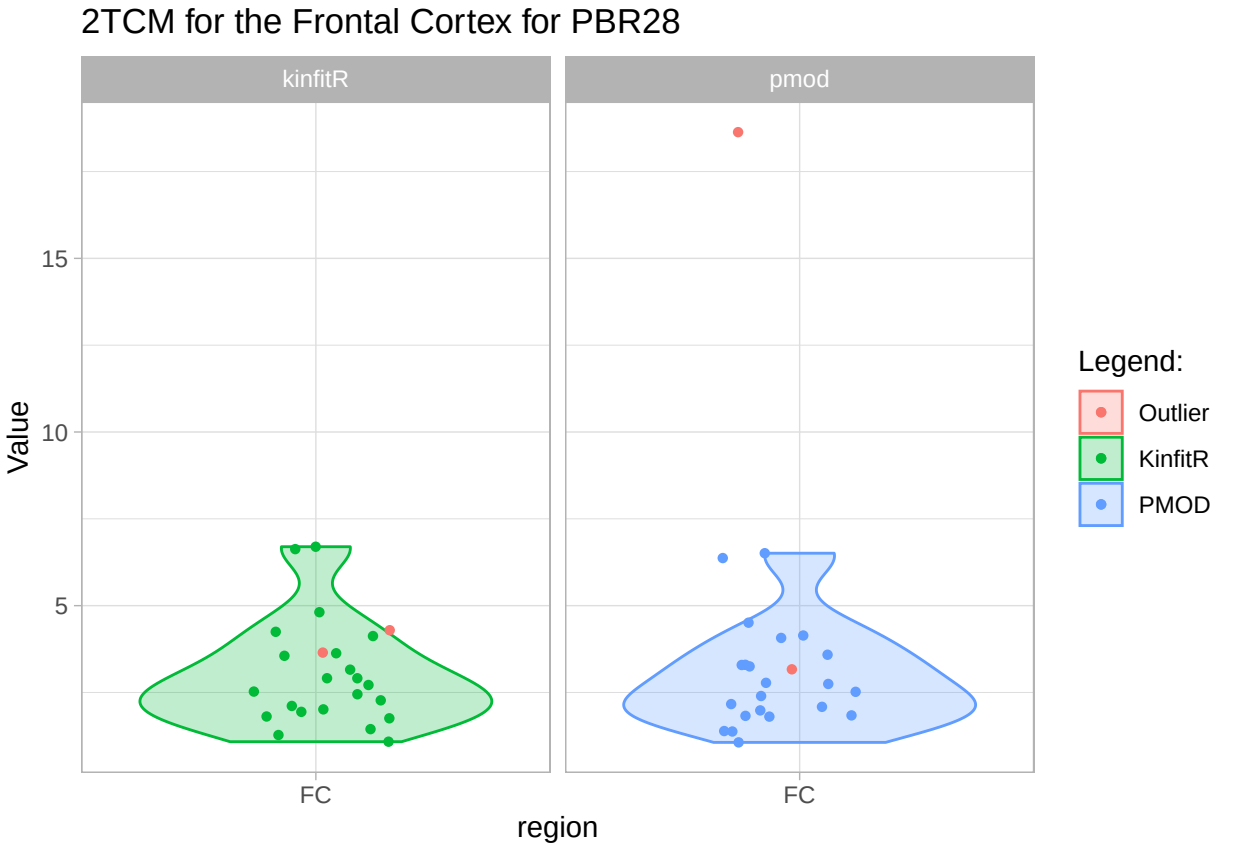
```
outlier <- macro %>%
  filter(subjname == "rwrd") %>%
  filter(region == "FC") %>%
  filter(Ligand == "pbr28") %>%
  filter(Model == "2TCM")

par(mfrow=c(3,1))

macro %>%
  filter(Ligand == "pbr28") %>%
  filter(Model == "2TCM") %>%
  filter(region == "FC") %>%
  ggplot(aes(x = region, y = Value, colour = software, fill = software)) +
  geom_violin(alpha=0.25)+
  geom_dotplot(binaxis='y', stackdir='center', dotsize=1) +
  facet_wrap( ~ software) +
  geom_dotplot(data = outlier, aes(x = region, y = Value, fill = "darkred", color = "darkred"),binaxis=
 scale_fill_discrete(name = "Legend:", labels = c("Outlier", "KinfitR", "PMOD")) +
 scale_color_discrete(name = "Legend:", labels = c("Outlier", "KinfitR", "PMOD"))+
ggtitle("2TCM for the Frontal Cortex for PBR28")
```




```
macro %>%
  filter(Ligand == "pbr28") %>%
  filter(Model == "2TCM") %>%
  filter(region == "FC") %>%
  ggplot(aes(x = region, y = Value, colour = software, fill = software)) +
  geom_violin(alpha=0.25)+
  geom_point() +
  facet_wrap( ~ software) +
  geom_point(data = outlier, aes(x = region, y = Value, fill = "darkred", color = "darkred")) +
 scale_fill_discrete(name = "Legend:", labels = c("Outlier", "KinfitR", "PMOD")) +
 scale_color_discrete(name = "Legend:", labels = c("Outlier", "KinfitR", "PMOD"))+
ggtitle("2TCM for the Frontal Cortex for PBR28")
```




```
macro %>%
  filter(Ligand == "pbr28") %>%
  filter(Model == "2TCM") %>%
  filter(region == "FC") %>%
  filter(subjname != "rwrd") %>%
  ggplot(aes(x = region, y = Value, colour = software, fill = software)) +
  geom_violin(alpha=0.25)+
  geom_jitter(shape=16, position=position_jitter(0.2)) +
  facet_wrap( ~ software) +
  geom_jitter(data = outlier, aes(x = region, y = Value, fill = "darkred", color = "darkred"),shape=16,
 scale_fill_discrete(name = "Legend:", labels = c("Outlier", "KinfitR", "PMOD")) +
 scale_color_discrete(name = "Legend:", labels = c("Outlier", "KinfitR", "PMOD"))+
ggtitle("2TCM for the Frontal Cortex for PBR28")
```



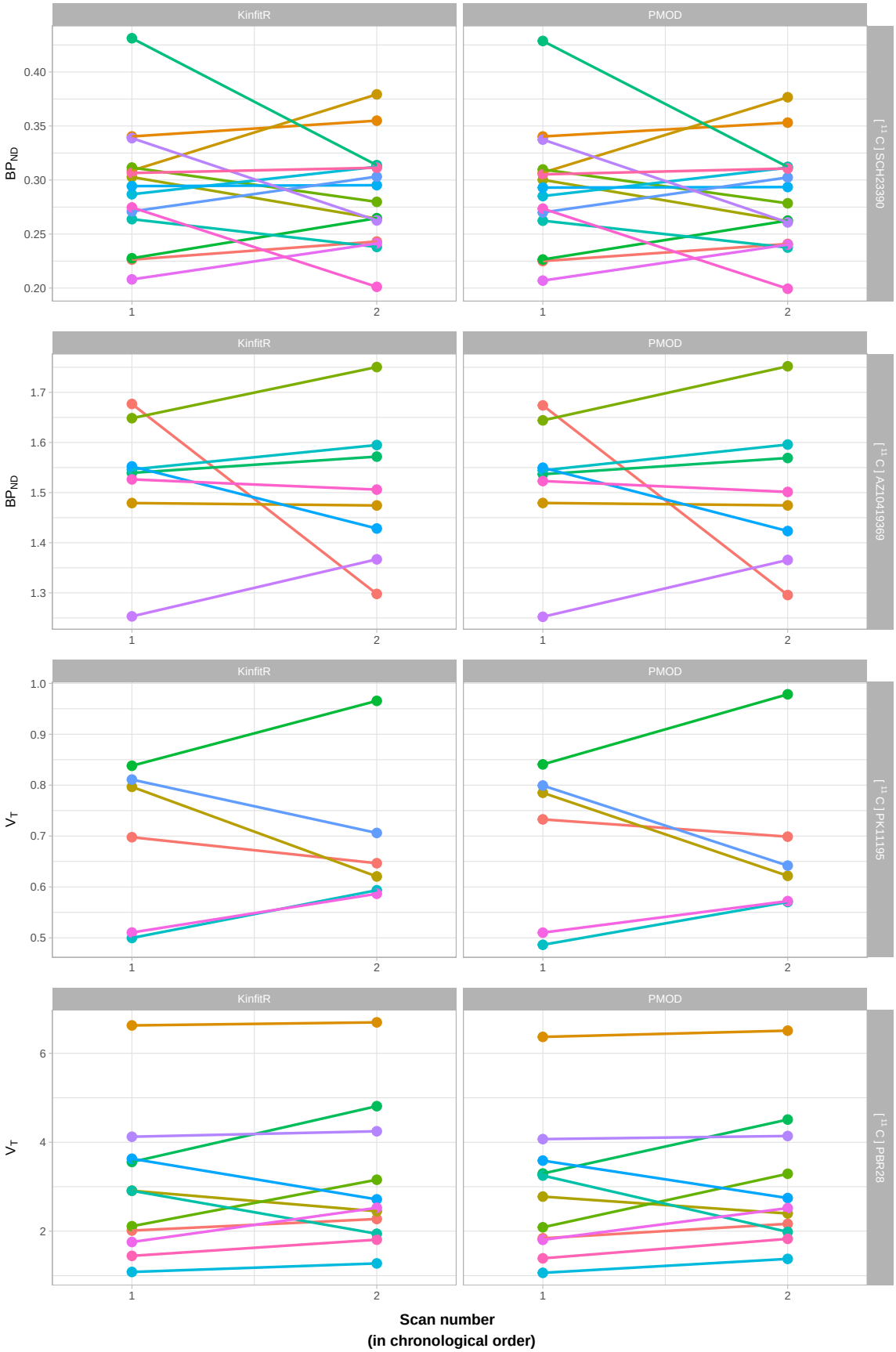
#exclusion of the outlier

```
macro <- macro %>%
  filter(subjname != "rwrd")
```

#Spaghetti plot for the Frontal Cortex

```
spaghetti <-macro %>%
  filter(region == "FC") %>%
  mutate(PETNo = as.integer(PETNo)) %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "az", replacement = "AZ10419369")) %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "sch", replacement = "SCH23390"))%>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "pk", replacement = "PK11195")) %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "pbr28", replacement = "PBR28")) %>%
  mutate(software = str_replace(string = software, pattern = "pmod", replacement = "PMOD")) %>%
  mutate(software = str_replace(string = software, pattern = "kinfitR", replacement = "KinfitR")) %>%
  mutate(Ligand = factor(Ligand, levels = c("SCH23390","PBR28","PK11195","AZ10419369"), labels = c("'['

spaghetti_pk <- spaghetti %>%
  filter(Ligand == "'['~{}^11~'C'~']'~plain(PK11195)") %>%
    filter(Model == "2TCM") %>%
 ggplot(aes(x = PETNo, y = Value,
            group = subjname, colour=subjname)) +
  geom_point(size = 3.3) +
  geom_smooth(method = 'lm', se = FALSE) +
  scale_x_continuous(limits = c(0.75, 2.25), breaks = c(1,2)) +
  facet_grid( Ligand ~ software, scales = "free", labeller=label_parsed) +
```

```
  theme(legend.position = "none")+
  labs(y = expression(V[T])) +
  theme(axis.title.x = element_blank())

spaghetti_az <- spaghetti %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(AZ10419369)") %>%
    filter(Model == "SRTM") %>%
ggplot(aes(x = PETNo, y = Value,
           group = subjname, colour=subjname)) +
  geom_point(size = 3.3) +
  geom_smooth(method = 'lm', se = FALSE) +
  scale_x_continuous(limits = c(0.75, 2.25), breaks = c(1,2)) +
  facet_grid(Ligand ~ software, scales = "free", labeller=label_parsed) +
  theme(legend.position = "none")+
  labs(y = expression(BP[ND]))+
  theme(axis.title.x = element_blank())

spaghetti_pbr <- spaghetti %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(PBR28)") %>%
  filter(Model == "2TCM") %>%
 ggplot(aes(x = PETNo, y = Value,
           group = subjname, colour=subjname)) +
  geom_point(size = 3.3) +
  geom_smooth(method = 'lm', se = FALSE) +
  scale_x_continuous(limits = c(0.75, 2.25), breaks = c(1,2)) +
  facet_grid(Ligand ~ software, scales = "free", labeller=label_parsed) +
  theme(legend.position = "none")+
  labs(y = expression(V[T])) +
  theme(axis.title.x = element_blank())



spaghetti_sch <- spaghetti %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(SCH23390)") %>%
  filter(Model == "SRTM") %>%
 ggplot(aes(x = PETNo, y = Value,
           group = subjname, colour=subjname)) +
  geom_point(size = 3.3) +
  geom_smooth(method = 'lm', se = FALSE) +
  scale_x_continuous(limits = c(0.75, 2.25), breaks = c(1,2)) +
  facet_grid(Ligand ~ software, scales = "free", labeller=label_parsed) +
  theme(legend.position = "none")+
  labs(y = expression(BP[ND])) +
  theme(axis.title.x = element_blank())


spaghetti_plot_two <- plot_grid(spaghetti_sch,spaghetti_az, spaghetti_pk,spaghetti_pbr, nrow = 4, align

x.grob <- textGrob("Scan number \n (in chronological order)",
                   gp=gpar(fontface="bold", col="black", fontsize=12))

grid.arrange(arrangeGrob(spaghetti_plot_two, bottom = x.grob))
```


KinfitR
PMOD
[11 C] SCH23390
[11 C] AZ10419369
[11 C] PK11195
[11 C] PBR28
BPND
VT
0.40
0.35
0.30
0.25
0.20
1.7
1.6
1.5
1.4
1.3
1.0
0.9
0.8
0.7
0.6
0.5
6
4
2
1
2
Scan number
(in chronological order)

```
# spag <- grid.arrange(arrangeGrob(spaghetti_plot_two, bottom = x.grob))
#
# ggsave(filename = "spaghetti.pdf", plot = spag, width = 170, height = 225, units = "mm", dpi = 300)
```

Split into reference tissue models and invasive models

```
ref <- macro %>%
  filter(measure == "bp")

aif <- macro %>%
  filter(measure == "Vt")
```

##Comparison between kinfitr and PMOD - reference tissue models

```
#preparing the data for trt.

Corr_ref <- ref %>%
  select(Ligand, region, Model, PET, software, Value) %>%
  group_by(Ligand, Model, region) %>%
  spread(software, Value) %>%
  mutate(Cor = cor(kinfitR, pmod)) %>%
  gather(key = software, value = Value, kinfitR:pmod) %>%
  group_by(Ligand, Model, region) %>%
  summarise(cormean = mean(Cor)) %>%
  rename(Cor = cormean) %>%
  mutate(region = case_when(
    region == "OC" ~ "Cor_1",
    region == "STR" ~ "Cor_1",
    TRUE ~ "Cor_2"
  ))  %>%
  spread(region, Cor) %>%
  ungroup()

Bias_ref <- ref %>%
  select(Ligand, region, Model, PET, software, Value) %>%
  group_by(Ligand, Model, region) %>%
  spread(software, Value) %>%
  mutate(Bias = (kinfitR-pmod)/pmod) %>%
  mutate(Bias = Bias * 100) %>%
  gather(key = software, value = Value, kinfitR:pmod) %>%
  group_by(Ligand, Model, region) %>%
  summarise(Bias = mean(Bias)) %>%
  mutate(region = case_when(
    region == "OC" ~ "Bias_1",
    region == "STR" ~ "Bias_1",
    TRUE ~ "Bias_2"
  ))  %>%
  spread(region, Bias) %>%
  ungroup()

ref <- ref %>%
  select(Ligand, region, Model, PET, software, Value) %>%
  group_by(Ligand, Model, region) %>%
  nest(.key = "data")
```

```r
#Using trt from the relfeas package to obtain ICC values
#Note: the values were not arranged by the "subjectname+PETNo" or "PET" variable
#Therefore, I had to use the "rater" argument of trt to specify "software", as
#the default behaviour is to take the value under as the second rater.

table_1 <- ref %>%
  group_by(Ligand, Model, region) %>%
  mutate(trt = map(data, ~relfeas::trt(.x,
                                       values = "Value",
                                       cases = "PET",
                                       rater = "software")),
         trt_tidy = map(trt, c("tidy"))) %>%
  select(trt_tidy) %>%
  unnest()

#Renaming OC and STR "Region 1" and making FC "Region 2"

table_1 <- table_1 %>%
  select(Ligand, Model, region, icc) %>%
  ungroup() %>%
  mutate(region = case_when(
    region == "OC" ~ "ICC (Region 1)",
    region == "STR" ~ "ICC (Region 1)",
    TRUE ~ "ICC (Region 2)"
  ))


#Rename the Ligands and then use Spread() on the regions and the ICC

table_1 <- table_1 %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "az", replacement = "AZ10419369")) %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "sch", replacement = "SCH23390")) %>%
  spread(region, icc) %>%
  mutate("Cor (Region 1)" = Corr_ref$Cor_1) %>%
  mutate("Cor (Region 2)" = Corr_ref$Cor_2) %>%
  mutate("Bias (Region 1)" = Bias_ref$Bias_1) %>%
  mutate("Bias (Region 2)" = Bias_ref$Bias_2) %>%
  arrange(Ligand, desc(Model))

# kable(table_1, format = "latex", booktabs = T,  digits = 3, escape = F) %>%
#   kable_styling(latex_options = c("striped"),
#                 full_width = F) %>%
#   footnote(symbol = c("Region 1 corresponds to the Occipital cortex in the case of AZ10419369 And the

# save_kable(table_1, 'figs/table_1.pdf')
```

Comparison between kinfitr and PMOD - models requiring blood sampling

```r
Corr_aif <- aif %>%
  select(Ligand, region, Model, PET, software, Value) %>%
  group_by(Ligand, Model, region) %>%
  spread(software, Value) %>%
```

```
 mutate(Cor = cor(kinfitR, pmod)) %>%
  gather(key = software, value = Value, kinfitR:pmod) %>%
  group_by(Ligand, Model, region) %>%
  summarise(cormean = mean(Cor)) %>%
  rename(Cor = cormean) %>%
  mutate(region = ifelse(region == "THA", "Cor_1", "Cor_2"))%>%
  spread(region, Cor) %>%
  ungroup()

Bias_aif <- aif %>%
  select(Ligand, region, Model, PET, software, Value) %>%
  group_by(Ligand, Model, region) %>%
  spread(software, Value) %>%
  mutate(Bias = (kinfitR-pmod)/pmod) %>%
  mutate(Bias = Bias * 100) %>%
  gather(key = software, value = Value, kinfitR:pmod) %>%
  group_by(Ligand, Model, region) %>%
  summarise(Bias = mean(Bias)) %>%
  mutate(region = ifelse(region == "THA", "Bias_1", "Bias_2"))%>%
  spread(region, Bias) %>%
  ungroup()

aif <- aif %>%
  select(Ligand, region, Model, PET, software, Value ) %>%
  group_by(Ligand, Model, region) %>%
  nest(.key = "data")

#Using trt from the relfeas package to obtain ICC values
#Note: the values were not arranged by the "subjectname+PETNo" or "PET" variable
#Therefore, I had to use the "rater" argument of trt to specify "software", as
#the default behaviour is to take the value under as the second rater.

table_2 <- aif %>%
  group_by(Ligand, Model, region) %>%
  mutate(trt = map(data, ~relfeas::trt(.x,
                                       values = "Value",
                                       cases = "PET",
                                       rater = "software")),
         trt_tidy = map(trt, c("tidy"))) %>%
  select(trt_tidy) %>%
  unnest()

#Renaming THA = Thalamus and FC = Frontal Cortex

table_2 <- table_2 %>%
  select(Ligand, Model, region, icc) %>%
  ungroup() %>%
  mutate(region = str_replace(string = region, pattern = "THA",
                              replacement = "ICC (Region 1)")) %>%
  mutate(region = str_replace(string = region, pattern = "FC",
                              replacement = "ICC (Region 2)"))
```

```
#Rename the Ligands and then use Spread() on the regions and the ICC

table_2 <- table_2 %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "pk", replacement = "PK11195")) %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "pbr28", replacement = "PBR28")) %>%
  spread(region, icc) %>%
  mutate("Cor (Region 1)" = Corr_aif$Cor_1) %>%
  mutate("Cor (Region 2)" = Corr_aif$Cor_2) %>%
  mutate("Bias (Region 1)" = Bias_aif$Bias_1) %>%
  mutate("Bias (Region 2)" = Bias_aif$Bias_2)

# kable(table_2, format = "latex", booktabs = T, digits = 3) %>%
#   kable_styling(latex_options = c("striped", "condensed", "scale_down"),
#                 full_width = F)

# save_kable(table_2, 'figs/table_2.pdf')
```

New combined tables 1 and 2

```
combo <- rbind(table_2, table_1) %>%
mutate(Ligand = str_replace(string = Ligand, pattern = "AZ10419369", replacement = "[$^{11}$C]AZ1041936
  mutate(Ligand = str_replace(string = Ligand, pattern = "SCH23390", replacement = "[$^{11}$C]SCH23390"
  mutate(Ligand = str_replace(string = Ligand, pattern = "PK11195", replacement = "[$^{11}$C]PK11195"))
  mutate(Ligand = str_replace(string = Ligand, pattern = "PBR28", replacement = "[$^{11}$C]PBR28"))


# kable(combo, format = "latex", booktabs = T,  digits = 2, escape = F,
#               caption = "Agreement between KinfitR and PMOD",
#       col.names = c("Ligand", "Model", "Region 1", "Region 2", "Region 1",
#                     "Region 2", "Bias 1", "Bias 2"), align= 'c') %>%
# kable_styling(full_width = F) %>%
# collapse_rows(columns = 1, latex_hline = "major", valign = "middle") %>%
# pack_rows("Invasive", 1, 6) %>%
# pack_rows("Non-Invasive", 7, 12) %>%
# add_header_above(c(" " = 2, "ICC" = 2, "Pearson's r" = 2, "Bias (%)" = 2))
#
# kable(combo, format = "latex", booktabs = T,  digits = 2, escape = F,
#               caption = "Agreement between KinfitR and PMOD",
#       col.names = c("Ligand", "Model", "Region 1", "Region 2", "Region 1",
#                     "Region 2", "Bias 1", "Bias 2"), align= 'c') %>%
# kable_styling(full_width = F, latex_options = "scale_down") %>%
# collapse_rows(columns = 1, latex_hline = "major", valign = "middle") %>%
# pack_rows("Invasive", 1, 6) %>%
# pack_rows("Non-Invasive", 7, 12) %>%
# add_header_above(c(" " = 2, "ICC" = 2, "Pearson's r" = 2, "Bias (%)" = 2)) %>%
# kable_as_image(.)

#save_kable did not work! Perhaps something in the latex code of kable_extra is
#preventing save_kable from working properly?

# mix <- kable(combo, format = "latex", booktabs = T,  digits = 2, escape = F,
#               caption = "Agreement between KinfitR and PMOD",
#       col.names = c("Ligand", "Model", "Region 1", "Region 2", "Region 1",
```

```
#                       "Region 2", "Bias 1", "Bias 2"), align= 'c') %>%
# kable_styling(full_width = F, latex_options = "scale_down") %>%
# collapse_rows(columns = 1, latex_hline = "major", valign = "middle") %>%
# pack_rows("Invasive", 1, 6) %>%
# pack_rows("Non-Invasive", 7, 12) %>%
# add_header_above(c(" " = 2, "ICC" = 2, "Pearson's r" = 2, "Bias (%)" = 2))
#
# save_kable(mix, 'table_1.pdf')
```

Comparison of the models

This figure will be included in the supplementary material.

The first figure compares the reference tissue models

```
ref_mod <- ref %>%
  unnest() %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "az", replacement = "AZ10419369")) %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "sch", replacement = "SCH23390"))%>%
  mutate(software = str_replace(string = software, pattern = "pmod", replacement = "PMOD")) %>%
  mutate(software = str_replace(string = software, pattern = "kinfitR", replacement = "KinfitR")) %>%
  mutate(Ligand = factor(Ligand, levels = c("SCH23390","AZ10419369"), labels = c("'[' ~ {}^11 ~ 'C' ~ '

az_srtm_OC <- ref_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(AZ10419369)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, SRTM) %>%
  select(- MRTM2, -"ref Logan") %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "OC") %>%
  mutate(Model = replicate(length(PET), "SRTM")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "OC",
                               replacement = "Occipital cortex")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

az_srtm_FC <- ref_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(AZ10419369)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, SRTM) %>%
  select(- MRTM2, -"ref Logan") %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "FC") %>%
  mutate(Model = replicate(length(PET), "SRTM")) %>%
  ungroup() %>%
```

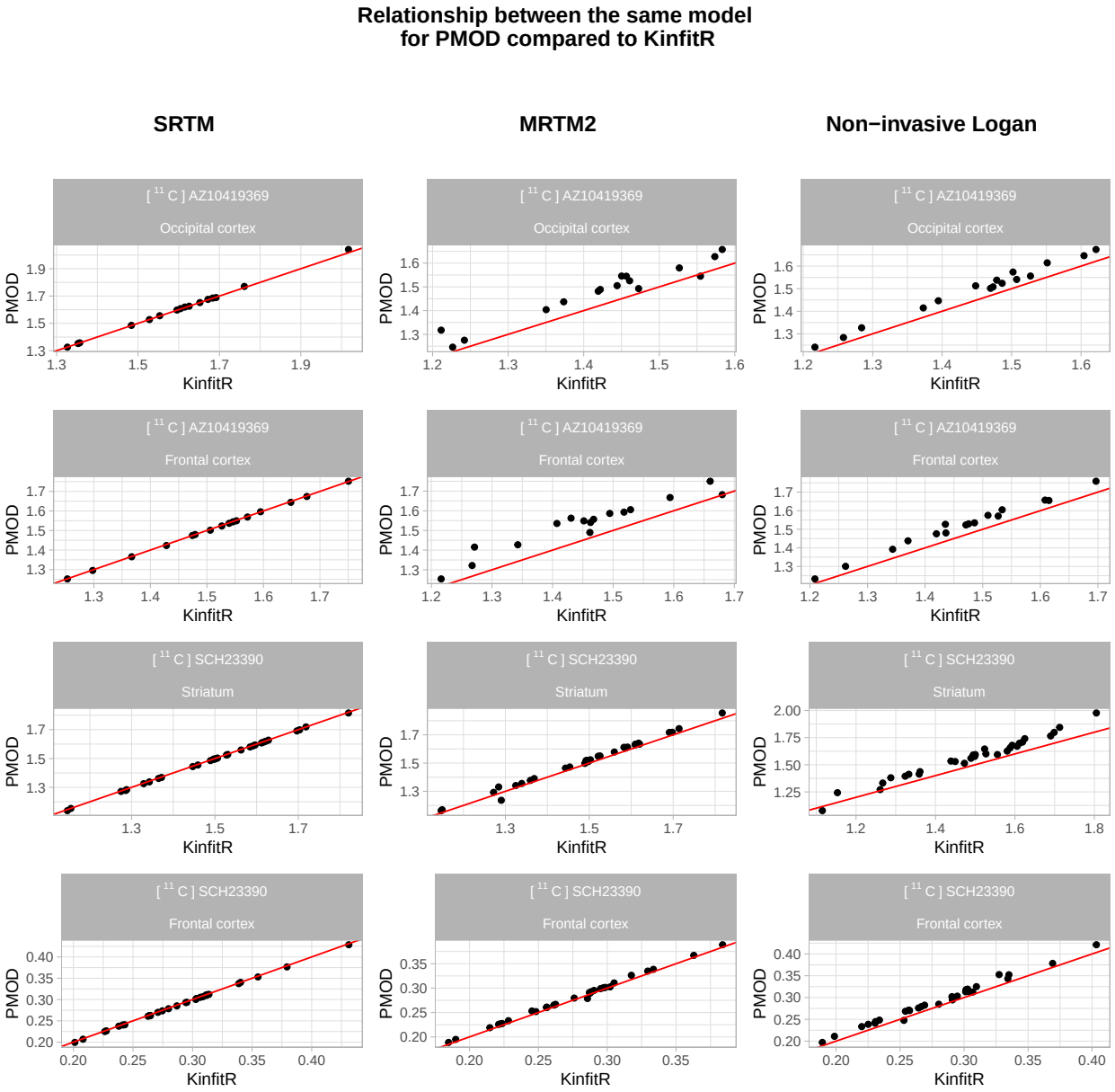
```
   mutate(region = str_replace(string = region, pattern = "FC",
                               replacement = "Frontal cortex")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

az_mrtm2_OC <- ref_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(AZ10419369)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, MRTM2) %>%
  select(- SRTM, -"ref Logan") %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "OC") %>%
  mutate(Model = replicate(length(PET), "MRTM2")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "OC",
                               replacement = "Occipital cortex")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

az_mrtm2_FC <- ref_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(AZ10419369)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, MRTM2) %>%
  select(- SRTM, -"ref Logan") %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "FC") %>%
  mutate(Model = replicate(length(PET), "MRTM2")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "FC",
                               replacement = "Frontal cortex")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

az_ref_logan_OC <- ref_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(AZ10419369)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, "ref Logan") %>%
  select(- MRTM2, -SRTM) %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
```

```
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "OC") %>%
  mutate(Model = replicate(length(PET), "ref Logan")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "OC",
                               replacement = "Occipital cortex")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

az_ref_logan_FC <- ref_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(AZ10419369)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, "ref Logan") %>%
  select(- MRTM2, -SRTM) %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "FC") %>%
  mutate(Model = replicate(length(PET), "ref Logan")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "FC",
                               replacement = "Frontal cortex")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

sch_srtm_STR <- ref_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(SCH23390)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, SRTM) %>%
  select(- MRTM2, -"ref Logan") %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "STR") %>%
  mutate(Model = replicate(length(PET), "SRTM")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "STR",
                               replacement = "Striatum")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

sch_srtm_FC <- ref_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(SCH23390)") %>%
  group_by(Ligand, region, PET) %>%
```

```
  spread(software, SRTM) %>%
  select(- MRTM2, -"ref Logan") %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "FC") %>%
  mutate(Model = replicate(length(PET), "SRTM")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "FC",
                               replacement = "Frontal cortex")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

sch_mrtm2_STR <- ref_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(SCH23390)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, MRTM2) %>%
  select(- SRTM, -"ref Logan") %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "STR") %>%
  mutate(Model = replicate(length(PET), "MRTM2")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "STR",
                               replacement = "Striatum")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

sch_mrtm2_FC <- ref_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(SCH23390)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, MRTM2) %>%
  select(- SRTM, -"ref Logan") %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "FC") %>%
  mutate(Model = replicate(length(PET), "MRTM2")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "FC",
                               replacement = "Frontal cortex")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  theme(plot.title = element_text(hjust = 0.5)) +
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))
```

```
sch_ref_logan_STR <- ref_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(SCH23390)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, "ref Logan") %>%
  select(- MRTM2, -SRTM) %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "STR") %>%
  mutate(Model = replicate(length(PET), "ref Logan")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "STR",
                               replacement = "Striatum")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

sch_ref_logan_FC <- ref_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(SCH23390)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, "ref Logan") %>%
  select(- MRTM2, -SRTM) %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "FC") %>%
  mutate(Model = replicate(length(PET), "ref Logan")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "FC",
                               replacement = "Frontal cortex")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

srtm_plot <- plot_grid(az_srtm_OC,az_srtm_FC,sch_srtm_STR,sch_srtm_FC, ncol =1)

srtm_title <- ggdraw() + draw_label("SRTM", fontface='bold')

srtm_plot <- plot_grid(srtm_title, srtm_plot, ncol = 1, rel_heights=c(0.1, 1))

mrtm2_plot <- plot_grid(az_mrtm2_OC,az_mrtm2_FC,sch_mrtm2_STR,sch_mrtm2_FC, ncol =1)

mrtm2_title <- ggdraw() + draw_label("MRTM2", fontface='bold')

mrtm2_plot <- plot_grid(mrtm2_title, mrtm2_plot, ncol = 1, rel_heights=c(0.1, 1))

ref_plot <- plot_grid(az_ref_logan_OC,az_ref_logan_FC,sch_ref_logan_STR,
                      sch_ref_logan_FC, ncol =1)
```

```
ref_title <- ggdraw() + draw_label("Non-invasive Logan", fontface='bold')

ref_plot <- plot_grid(ref_title, ref_plot, ncol = 1, rel_heights=c(0.1, 1))

combined_plot <- plot_grid(srtm_plot, mrtm2_plot, ref_plot, ncol = 3)

title <- ggdraw() + draw_label("Relationship between the same model \nfor PMOD compared to KinfitR", fo

plot_grid(title, combined_plot , ncol = 1, rel_heights=c(0.1, 1))
```



The next figure shows the relationship between kinfitr and pmod for the models that require arterial blood sampling

```r
aif_mod <- aif %>%
  unnest() %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "pk", replacement = "PK11195")) %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "pbr28", replacement = "PBR28")) %>%
  mutate(software = str_replace(string = software, pattern = "pmod", replacement = "PMOD")) %>%
  mutate(software = str_replace(string = software, pattern = "kinfitR", replacement = "KinfitR")) %>%
  mutate(Ligand = factor(Ligand, levels = c("PBR28","PK11195"), labels = c("'[' ~ {}^11 ~ 'C' ~ ']' ~ p

pk_2tcm_tha <- aif_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(PK11195)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, "2TCM") %>%
  select(- Logan, -MA1) %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "THA") %>%
  mutate(Model = replicate(length(PET), "2TCM")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "THA",
                               replacement = "Thalamus")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

pk_logan_tha <- aif_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(PK11195)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, Logan) %>%
  select(- "2TCM", -MA1) %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "THA") %>%
  mutate(Model = replicate(length(PET), "Logan")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "THA",
                               replacement = "Thalamus")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

pk_ma1_tha <- aif_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(PK11195)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, MA1) %>%
  select(- "2TCM", -Logan) %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
```

```
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "THA") %>%
  mutate(Model = replicate(length(PET), "MA1")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "THA",
                               replacement = "Thalamus")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

pk_2tcm_fc <- aif_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(PK11195)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, "2TCM") %>%
  select(- Logan, -MA1) %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "FC") %>%
  mutate(Model = replicate(length(PET), "2TCM")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "FC",
                               replacement = "Frontal Cortex")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

pk_logan_fc <- aif_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(PK11195)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, Logan) %>%
  select(- "2TCM", -MA1) %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "FC") %>%
  mutate(Model = replicate(length(PET), "Logan")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "FC",
                               replacement = "Frontal Cortex")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

pk_ma1_fc <- aif_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(PK11195)") %>%
```

```
  group_by(Ligand, region, PET) %>%
  spread(software, MA1) %>%
  select(- "2TCM", -Logan) %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "FC") %>%
  mutate(Model = replicate(length(PET), "MA1")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "FC",
                               replacement = "Frontal Cortex")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

pbr_2tcm_tha <- aif_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(PBR28)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, "2TCM") %>%
  select(- Logan, -MA1) %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "THA") %>%
  mutate(Model = replicate(length(PET), "2TCM")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "THA",
                               replacement = "Thalamus")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

pbr_logan_tha <- aif_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(PBR28)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, Logan) %>%
  select(- "2TCM", -MA1) %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "THA") %>%
  mutate(Model = replicate(length(PET), "Logan")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "THA",
                               replacement = "Thalamus")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))
```

```
pbr_ma1_tha <- aif_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(PBR28)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, MA1) %>%
  select(- "2TCM", -Logan) %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "THA") %>%
  mutate(Model = replicate(length(PET), "MA1")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "THA",
                               replacement = "Thalamus")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

pbr_2tcm_fc <- aif_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(PBR28)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, "2TCM") %>%
  select(- Logan, -MA1) %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "FC") %>%
  mutate(Model = replicate(length(PET), "2TCM")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "FC",
                               replacement = "Frontal Cortex")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

pbr_logan_fc <- aif_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(PBR28)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, Logan) %>%
  select(- "2TCM", -MA1) %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "FC") %>%
  mutate(Model = replicate(length(PET), "Logan")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "FC",
                               replacement = "Frontal Cortex")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
```

```
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

pbr_ma1_fc <- aif_mod %>%
  ungroup() %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(PBR28)") %>%
  group_by(Ligand, region, PET) %>%
  spread(software, MA1) %>%
  select(- "2TCM", -Logan) %>%
  summarize_at(vars(KinfitR, PMOD), funs(toString(unique(.[!is.na(.)])))) %>%
  mutate(KinfitR = as.double(KinfitR)) %>%
  mutate(PMOD = as.double(PMOD)) %>%
  filter(region == "FC") %>%
  mutate(Model = replicate(length(PET), "MA1")) %>%
  ungroup() %>%
   mutate(region = str_replace(string = region, pattern = "FC",
                               replacement = "Frontal Cortex")) %>%
  ggplot(aes(x = KinfitR, y = PMOD)) +
  geom_point() +
  geom_abline(slope = 1, intercept = 0, color = "red")+
  facet_grid(. ~ Ligand + region, labeller = labeller(Ligand = label_parsed))

two_tcm_plot <- plot_grid(pk_2tcm_tha,pk_2tcm_fc,pbr_2tcm_tha, pbr_2tcm_fc, ncol =1)

two_tcm_title <- ggdraw() + draw_label("2TCM", fontface='bold')

two_tcm_plot <- plot_grid(two_tcm_title, two_tcm_plot, ncol = 1, rel_heights=c(0.1, 1))


ma1_plot <- plot_grid(pk_ma1_tha,pk_ma1_fc,pbr_ma1_tha, pbr_ma1_fc, ncol =1)

ma1_title <- ggdraw() + draw_label("MA1", fontface='bold')

ma1_plot <- plot_grid(ma1_title, ma1_plot, ncol = 1, rel_heights=c(0.1, 1))

logan_plot <- plot_grid(pk_logan_tha,pk_logan_fc,pbr_logan_tha, pbr_logan_fc, ncol =1)

logan_title <- ggdraw() + draw_label("Invasive Logan", fontface='bold')

logan_plot <- plot_grid(logan_title, logan_plot, ncol = 1, rel_heights=c(0.1, 1))

combine_plot <- plot_grid(two_tcm_plot, ma1_plot, logan_plot, ncol = 3)

titles <- ggdraw() + draw_label("Relationship between the same model \nfor PMOD compared to KinfitR", fo

plot_grid(titles, combine_plot , ncol = 1, rel_heights=c(0.1, 1))
```

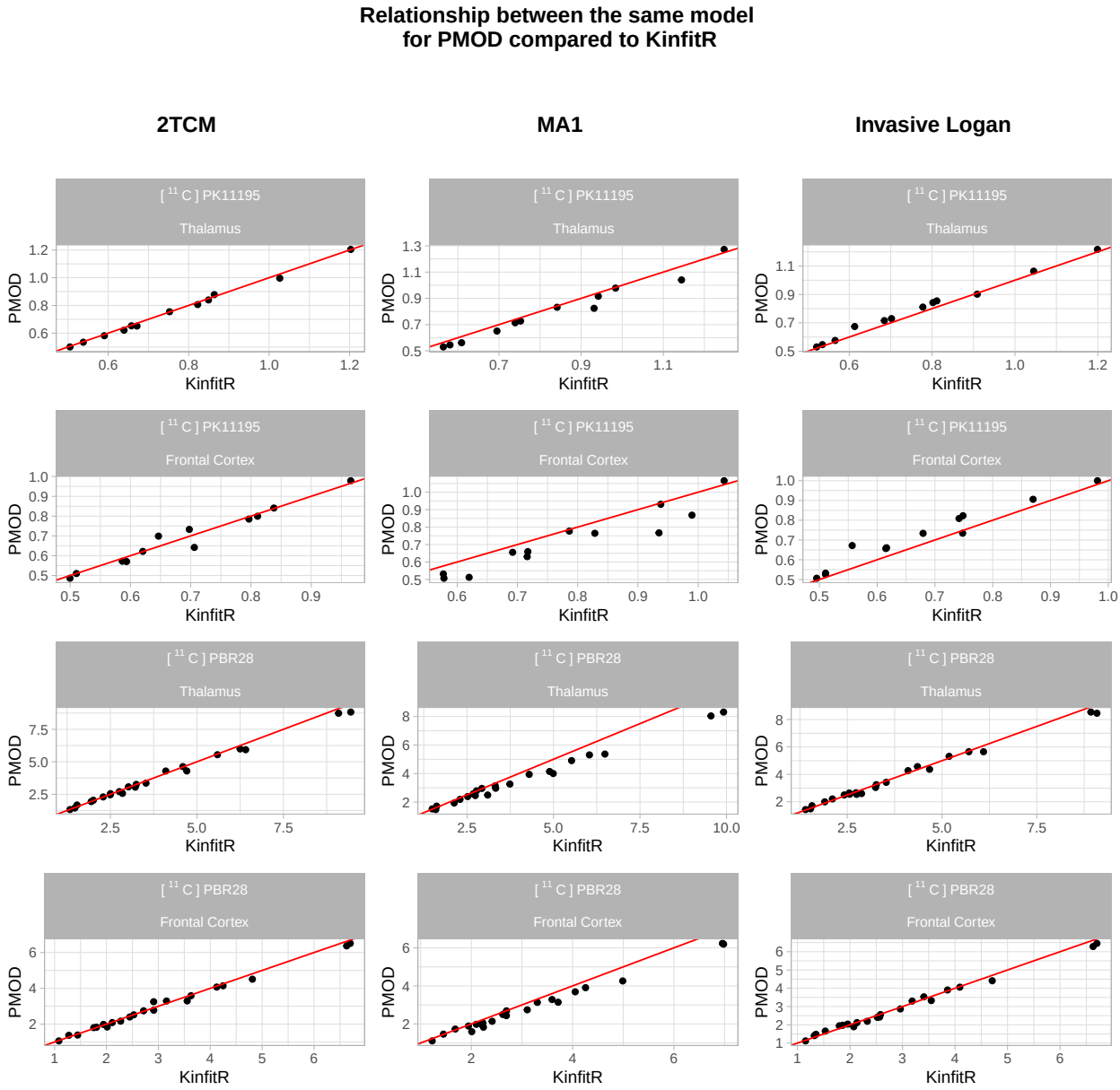


Table 3 - consistency test_retest

```
macro_sch <- macro %>%
  filter(Ligand == "sch") %>%
  filter(region == "STR")

macro_az <- macro %>%
  filter(Ligand == "az") %>%
  filter(region == "OC")

macro_aif <- macro %>%
  filter(measure == "Vt") %>%
```

```
  filter(region == "THA")

macro <- bind_rows(macro_sch, macro_aif, macro_az)


trt <- macro %>%
  select(software, Ligand, Model, Value, subjname, PETNo ) %>%
  group_by(Ligand, software, Model) %>%
  nest(.key = "data")

trt <- trt %>%
  group_by(Ligand, software, Model) %>%
  mutate(trt = map(data, ~relfeas::trt(.x,
                                       values = "Value",
                                       cases = "subjname",
                                       rater = "PETNo")),
         trt_tidy = map(trt, c("tidy")))

#Note: multiplied "VAR" by 100 so that it is a percentage

trt <- trt %>%
  select(trt_tidy) %>%
  unnest() %>%
  select(Ligand, Software = software, Model, Mean = mean, "CV" = cov, ICC = icc, "WSCV" = wscv, "AV" = a
  ungroup() %>%
  mutate(`AV` = `AV` *100) %>%
  mutate(`WSCV` = `WSCV` * 100) %>%
  mutate(`CV` = `CV` * 100) %>%
  mutate(Software = str_replace( string = Software, pattern = "pmod", replacement = "PMOD")) %>%
  mutate(Software = str_replace( string = Software, pattern = "kinfitR", replacement = "KinfitR")) %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "pk", replacement = "PK11195")) %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "pbr28", replacement = "PBR28")) %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "az", replacement = "AZ10419369")) %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "sch", replacement = "ASCH23390")) %>%
   mutate(Model = str_replace(string = Model, pattern = "SRTM", replacement = "aSRTM")) %>%
  mutate(Model = str_replace(string = Model, pattern = "ref Logan", replacement = "bref Logan")) %>%
  arrange(desc(Ligand), Model) %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "ASCH23390", replacement = "SCH23390")) %>%
  mutate(Model = str_replace(string = Model, pattern = "aSRTM", replacement = "SRTM")) %>%
  mutate(Model = str_replace(string = Model, pattern = "bref Logan", replacement = "ref Logan")) %>%
mutate(Ligand = str_replace(string = Ligand, pattern = "AZ10419369", replacement = "[$^{11}$C]AZ1041936
  mutate(Ligand = str_replace(string = Ligand, pattern = "SCH23390", replacement = "[$^{11}$C]SCH23390"
  mutate(Ligand = str_replace(string = Ligand, pattern = "PK11195", replacement = "[$^{11}$C]PK11195"))
  mutate(Ligand = str_replace(string = Ligand, pattern = "PBR28", replacement = "[$^{11}$C]PBR28"))

kable(trt, format = "latex", booktabs = TRUE,digits = c(0,0,0, 2, 1,2,1,1),
      escape = FALSE, caption = "Test-retest reliability of KinfitR and PMOD",  col.names = c("Ligand",
               "AV (\\%)") , align = 'c') %>%
kable_styling(full_width = F) %>%
collapse_rows(columns = 1, latex_hline = "major" ,valign = "middle") %>%
row_spec(2, extra_latex_after = "\\cline{2-8}") %>%
row_spec(4, extra_latex_after = "\\cline{2-8}") %>%
row_spec(8, extra_latex_after = "\\cline{2-8}") %>%
```

Table 1: Test-retest reliability of KinfitR and PMOD

Ligand	Software	Model	Mean	CV (%)	ICC	WSCV (%)	AV (%)
Invasive							
[^{11}C]PK11195	KinfitR	2TCM	0.76	27.1	0.75	13.9	18.9
	PMOD	2TCM	0.75	27.4	0.72	15.0	20.0
	KinfitR	Logan	0.76	27.2	0.79	12.9	17.2
	PMOD	Logan	0.79	26.2	0.80	12.2	16.2
	KinfitR	MA1	0.84	26.4	0.73	14.1	17.9
	PMOD	MA1	0.80	28.2	0.67	16.6	19.2
[^{11}C]PBR28	KinfitR	2TCM	3.84	59.6	0.91	18.4	25.1
	PMOD	2TCM	3.73	57.3	0.89	19.1	26.7
	KinfitR	Logan	3.75	57.4	0.91	17.7	24.4
	PMOD	Logan	3.68	54.8	0.88	19.4	26.5
	KinfitR	MA1	4.00	58.4	0.91	18.0	24.0
	PMOD	MA1	3.54	53.1	0.91	16.7	23.7
Non-Invasive							
[^{11}C]AZ10419369	KinfitR	SRTM	1.59	10.7	0.67	6.3	5.9
	PMOD	SRTM	1.60	11.0	0.67	6.5	5.9
	KinfitR	ref Logan	1.45	8.1	0.61	5.2	4.8
	PMOD	ref Logan	1.49	8.3	0.62	5.3	5.5
	KinfitR	MRTM2	1.42	8.2	0.52	5.9	4.7
	PMOD	MRTM2	1.48	8.0	0.59	5.2	5.5
[^{11}C]SCH23390	KinfitR	SRTM	1.49	11.1	0.83	4.6	5.0
	PMOD	SRTM	1.49	11.2	0.83	4.6	5.0
	KinfitR	ref Logan	1.48	11.3	0.82	4.8	5.3
	PMOD	ref Logan	1.56	12.3	0.80	5.6	7.0
	KinfitR	MRTM2	1.49	11.1	0.83	4.6	4.9
	PMOD	MRTM2	1.51	11.3	0.82	4.9	5.4

```
row_spec(10, extra_latex_after = "\\cline{2-8}") %>%
row_spec(14, extra_latex_after = "\\cline{2-8}") %>%
row_spec(16, extra_latex_after = "\\cline{2-8}") %>%
row_spec(20, extra_latex_after = "\\cline{2-8}") %>%
row_spec(22, extra_latex_after = "\\cline{2-8}") %>%
pack_rows("Invasive", 1, 12) %>%
pack_rows("Non-Invasive", 13, 24)
```

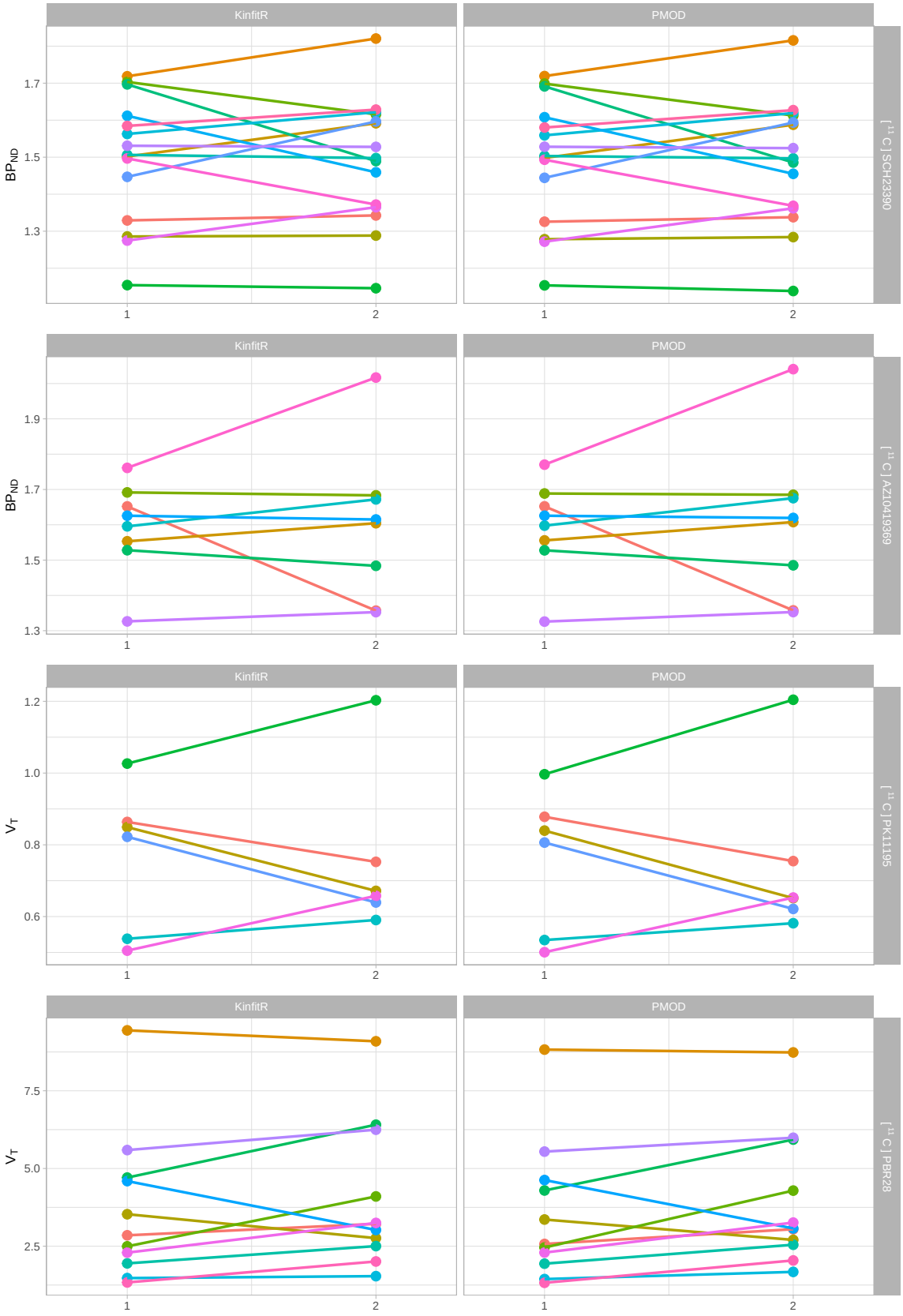
```
# kable(trt, format = "latex", booktabs = TRUE,digits = c(0,0,0, 2, 1,2,1,1),
#       escape = FALSE, caption = "Test-retest reliability of KinfitR and PMOD",  align = 'c') %>%
# kable_styling(full_width = F, latex_options = "scale_down") %>%
# collapse_rows(columns = 1, latex_hline = "major" ,valign = "middle") %>%
# row_spec(2, extra_latex_after = "\\cline{2-8}") %>%
# row_spec(4, extra_latex_after = "\\cline{2-8}") %>%
# row_spec(8, extra_latex_after = "\\cline{2-8}") %>%
# row_spec(10, extra_latex_after = "\\cline{2-8}") %>%
# row_spec(14, extra_latex_after = "\\cline{2-8}") %>%
# row_spec(16, extra_latex_after = "\\cline{2-8}") %>%
# row_spec(20, extra_latex_after = "\\cline{2-8}") %>%
# row_spec(22, extra_latex_after = "\\cline{2-8}") %>%
# pack_rows("Invasive", 1, 12) %>%
```

```
# pack_rows("Non-Invasive", 13, 24) %>%
# kable_as_image(.)


# test_retest <- kable(trt, format = "latex", booktabs = TRUE,digits = c(0,0,0, 2, 1,2,1,1),
#       escape = FALSE, align = 'c') %>%
# kable_styling(full_width = F) %>%
# collapse_rows(columns = 1, latex_hline = "major" ,valign = "middle") %>%
# row_spec(2, extra_latex_after = "\\cline{2-8}") %>%
# row_spec(4, extra_latex_after = "\\cline{2-8}") %>%
# row_spec(8, extra_latex_after = "\\cline{2-8}") %>%
# row_spec(10, extra_latex_after = "\\cline{2-8}") %>%
# row_spec(14, extra_latex_after = "\\cline{2-8}") %>%
# row_spec(16, extra_latex_after = "\\cline{2-8}") %>%
# row_spec(20, extra_latex_after = "\\cline{2-8}") %>%
# row_spec(22, extra_latex_after = "\\cline{2-8}") %>%
# pack_rows("Invasive", 1, 12) %>%
# pack_rows("Non-Invasive", 13, 24)
#
# save_kable(test_retest, 'table_2.pdf')
```

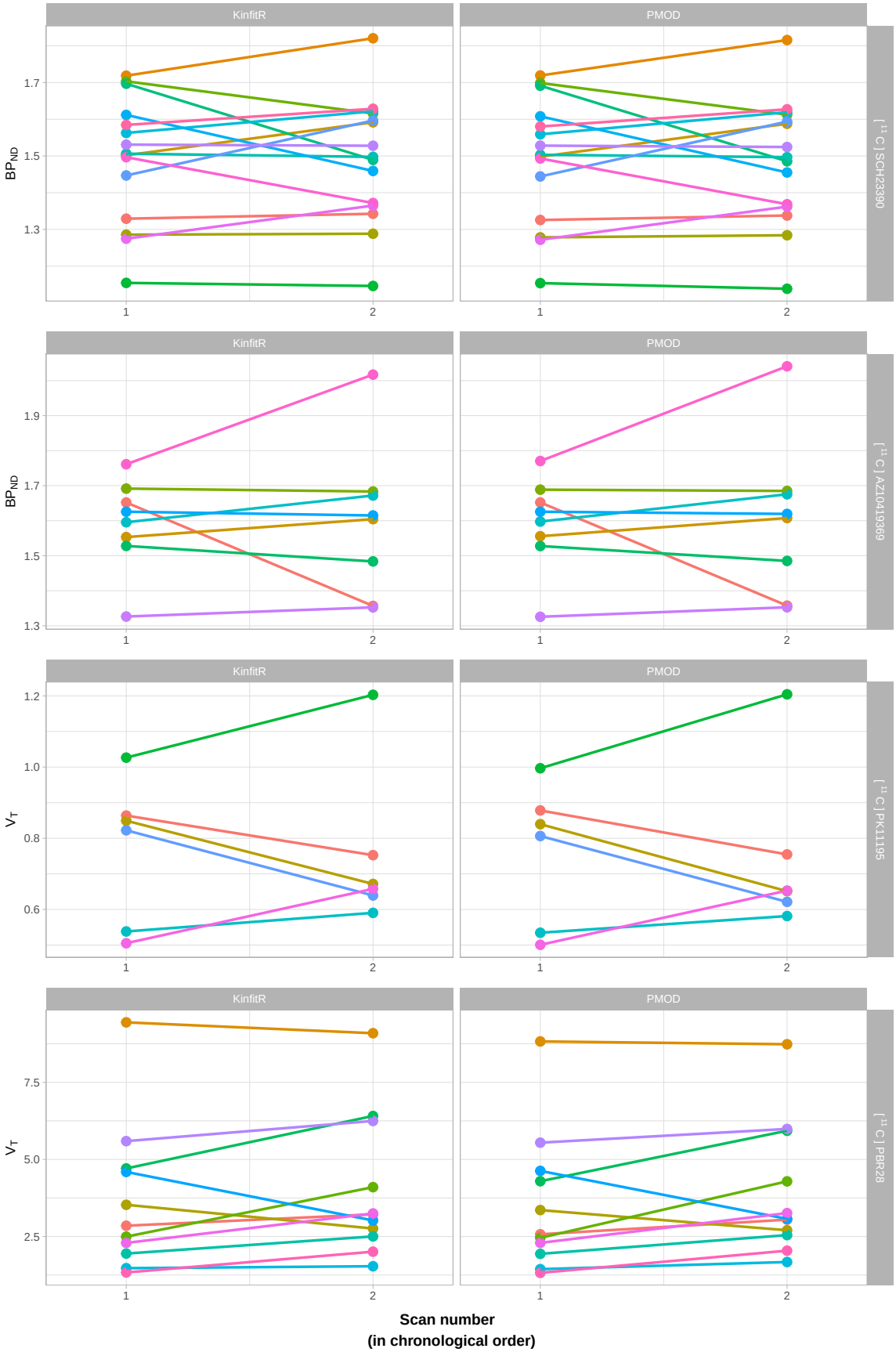
Spaghetti plot - The occipital cortex

```
spaghetti <-macro %>%
  mutate(PETNo = as.integer(PETNo)) %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "az", replacement = "AZ10419369")) %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "sch", replacement = "SCH23390"))%>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "pk", replacement = "PK11195")) %>%
  mutate(Ligand = str_replace(string = Ligand, pattern = "pbr28", replacement = "PBR28")) %>%
  mutate(software = str_replace(string = software, pattern = "pmod", replacement = "PMOD")) %>%
  mutate(software = str_replace(string = software, pattern = "kinfitR", replacement = "KinfitR")) %>%
  mutate(Ligand = factor(Ligand, levels = c("SCH23390","PBR28","PK11195","AZ10419369"), labels = c("'['

spaghetti_pk <- spaghetti %>%
  filter(Ligand == "'['~{}^11~'C'~']'~plain(PK11195)") %>%
    filter(Model == "2TCM") %>%
 ggplot(aes(x = PETNo, y = Value,
            group = subjname, colour=subjname)) +
  geom_point(size = 3.3) +
  geom_smooth(method = 'lm', se = FALSE) +
  scale_x_continuous(limits = c(0.75, 2.25), breaks = c(1,2)) +
  facet_grid( Ligand ~ software, scales = "free", labeller=label_parsed) +
  theme(legend.position = "none")+
  labs(y = expression(V[T])) +
  theme(axis.title.x = element_blank())

spaghetti_az <- spaghetti %>%
  filter(Ligand == "'['~{}^11~'C'~']'~plain(AZ10419369)") %>%
    filter(Model == "SRTM") %>%
ggplot(aes(x = PETNo, y = Value,
            group = subjname, colour=subjname)) +
  geom_point(size = 3.3) +
```

```
  geom_smooth(method = 'lm', se = FALSE) +
  scale_x_continuous(limits = c(0.75, 2.25), breaks = c(1,2)) +
  facet_grid(Ligand ~ software, scales = "free", labeller=label_parsed) +
  theme(legend.position = "none")+
  labs(y = expression(BP[ND]))+
  theme(axis.title.x = element_blank())

spaghetti_pbr <- spaghetti %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(PBR28)") %>%
  filter(Model == "2TCM") %>%
 ggplot(aes(x = PETNo, y = Value,
            group = subjname, colour=subjname)) +
  geom_point(size = 3.3) +
  geom_smooth(method = 'lm', se = FALSE) +
  scale_x_continuous(limits = c(0.75, 2.25), breaks = c(1,2)) +
  facet_grid(Ligand ~ software, scales = "free", labeller=label_parsed) +
  theme(legend.position = "none")+
  labs(y = expression(V[T])) +
  theme(axis.title.x = element_blank())



spaghetti_sch <- spaghetti %>%
  filter(Ligand == "'[' ~ {}^11 ~ 'C' ~ ']' ~ plain(SCH23390)") %>%
  filter(Model == "SRTM") %>%
 ggplot(aes(x = PETNo, y = Value,
            group = subjname, colour=subjname)) +
  geom_point(size = 3.3) +
  geom_smooth(method = 'lm', se = FALSE) +
  scale_x_continuous(limits = c(0.75, 2.25), breaks = c(1,2)) +
  facet_grid(Ligand ~ software, scales = "free", labeller=label_parsed) +
  theme(legend.position = "none")+
  labs(y = expression(BP[ND])) +
  theme(axis.title.x = element_blank())


spaghetti_plot_two <- plot_grid(spaghetti_sch,spaghetti_az, spaghetti_pk,spaghetti_pbr, nrow = 4, align

x.grob <- textGrob("Scan number \n (in chronological order)",
                   gp=gpar(fontface="bold", col="black", fontsize=12))

grid.arrange(arrangeGrob(spaghetti_plot_two, bottom = x.grob))
```


KinfitR
PMOD
[11 C] SCH23390
[11 C] AZ10419369
[11 C] PK11195
[11 C] PBR28
BPND
VT
1.7
1.5
1.3
1.9
1.2
1.0
0.8
0.6
7.5
5.0
2.5
1
2
Scan number
(in chronological order)

```
spag <- grid.arrange(arrangeGrob(spaghetti_plot_two, bottom = x.grob))
```


KinfitR
PMOD
[11 C] SCH23390
[11 C] AZ10419369
[11 C] PK11195
[11 C] PBR28
BPND
VT
1.7
1.5
1.3
1.9
1.2
1.0
0.8
0.6
7.5
5.0
2.5
1
2
Scan number
(in chronological order)

```
# ggsave(filename = "spaghetti.pdf", plot = spag, width = 170, height = 225, units = "mm", dpi = 300)

# ggsave(filename = "spaghetti.png", plot = spag, width = 170, height = 225, units = "mm", dpi = 300)
```

Microparameters

Load microparameters

```
micro_aif_pmod <- readRDS('Data_PMOD_RDS/micro_aif_pmod.rds') %>%
  mutate(PETNo = as.numeric(PETNo))%>%
  mutate(subjnumber = as.character(id))%>%
  rename(K1_pmod = K1, k2_pmod = k2, k3_pmod = k3, k4_pmod = k4) %>%
  select(- software)

micro_ref_pmod <- readRDS('Data_PMOD_RDS/micro_ref_pmod.rds') %>%
  mutate(PETNo = as.numeric(PETNo))%>%
  mutate(subjnumber = as.character(id))%>%
  rename(R1_pmod = R1, k2_pmod = k2) %>%
  select(-software)

micro_aif_kinfitr <- readRDS('Data_PMOD_RDS/micro_aif_kinfitr.rds')%>%
  mutate(subjnumber = as.character(id))%>%
  rename(K1_kinfitr = K1, k2_kinfitr = k2, k3_kinfitr = k3, k4_kinfitr = k4) %>%
  select(- software)

micro_ref_kinfitr <- readRDS('Data_PMOD_RDS/micro_ref_kinfitr.rds') %>%
  mutate(subjnumber = as.character(id))%>%
  rename(R1_kinfitr = R1, k2_kinfitr = k2) %>%
  select(- software)
```

Combine datasets

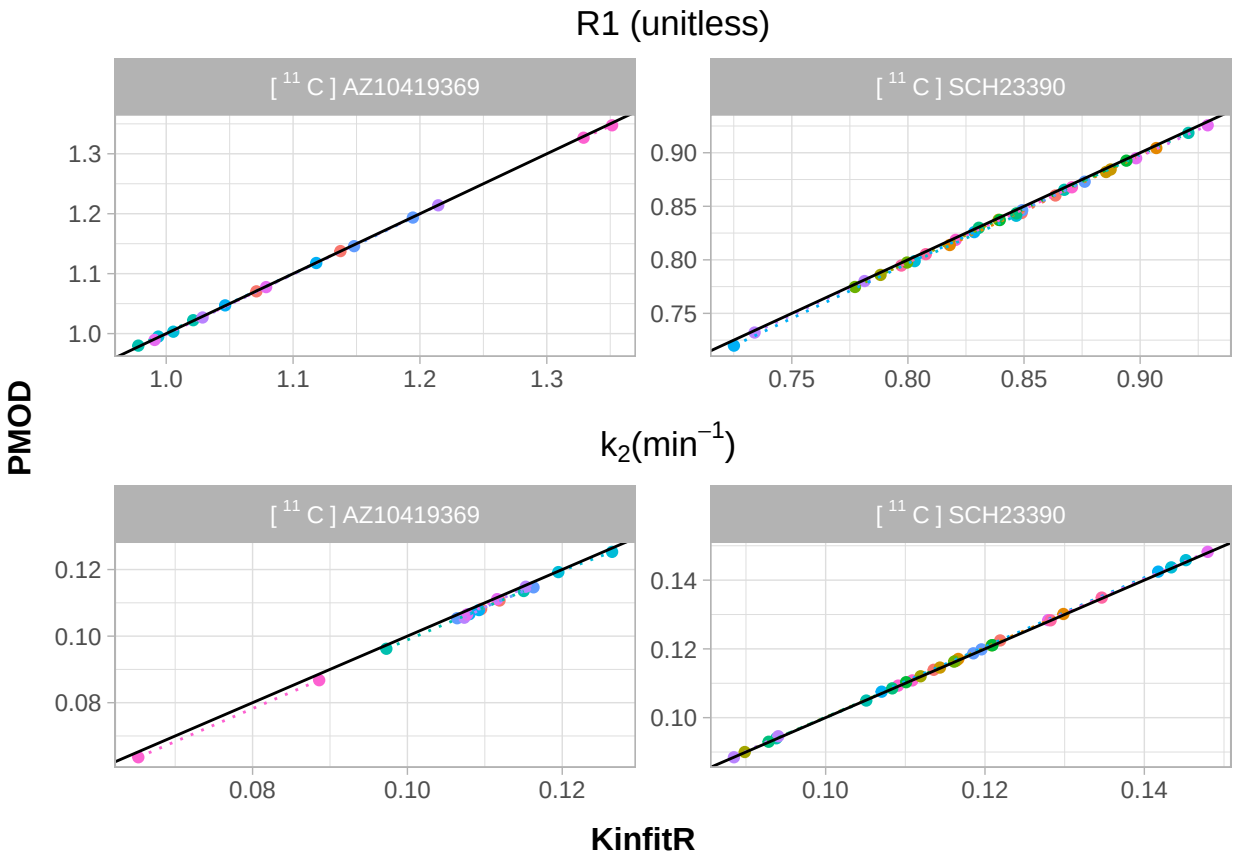
```
micro_ref <- inner_join(micro_ref_pmod, micro_ref_kinfitr)%>%
  arrange(Ligand) %>%
  mutate(Ligand = factor(Ligand, levels = c("AZ10419369","SCH23390"), labels = c("'['  ~ {}^11 ~ 'C' ~ '

micro_aif <- inner_join(micro_aif_pmod, micro_aif_kinfitr) %>%
  arrange(Ligand) %>%
  mutate(Ligand = factor(Ligand, levels = c("PBR28","PK11195"), labels = c("'['  ~ {}^11 ~ 'C' ~ ']' ~ pl
  filter(subjname != "rwrd")
```

Fig 2, microparameter dotplot with abline for srtm

Using the Occipital cortex ROI

```
R1 <- micro_ref %>%
  ggplot(aes(x = R1_kinfitr, y = R1_pmod, color = subjnumber)) +
  geom_point() +
  geom_line(aes(group=subjnumber), linetype="dotted") +
  geom_abline(slope = 1, intercept = 0) +
  facet_wrap( ~ Ligand, scales = "free", labeller=label_parsed)+ theme(legend.position = "none")+
  ggtitle("R1 (unitless)")+
```

```
  theme(plot.title = element_text(hjust = 0.5)) +
  theme(axis.title = element_blank())

k2_ref <- micro_ref %>%
  ggplot(aes(x = k2_kinfitr, y = k2_pmod, color = subjnumber)) +
  geom_point() +
  geom_line(aes(group=subjnumber), linetype="dotted") +
  geom_abline(slope = 1, intercept = 0) +
  facet_wrap( ~ Ligand, scales = "free", labeller=label_parsed)+ theme(legend.position = "none") +
  ggtitle(expression(paste (k[2], "(", min^-1, ")", sep = ' ')))+
  theme(plot.title = element_text(hjust = 0.5)) +
  theme(axis.title = element_blank())

plot_ref <- plot_grid(R1, k2_ref, nrow = 2, align = "v")

y.grob <- textGrob("PMOD",
                   gp=gpar(fontface="bold", col="black", fontsize=12), rot=90)

x.grob <- textGrob("KinfitR",
                   gp=gpar(fontface="bold", col="black", fontsize=12))

grid.arrange(arrangeGrob(plot_ref, left = y.grob, bottom = x.grob))
```




```
#  micro_reference <- grid.arrange(arrangeGrob(plot_ref, left = y.grob, bottom = x.grob))
# #
# # ggsave(filename = "micro_ref.pdf", plot = micro_reference, width = 170, height = 225, units = "mm",
```

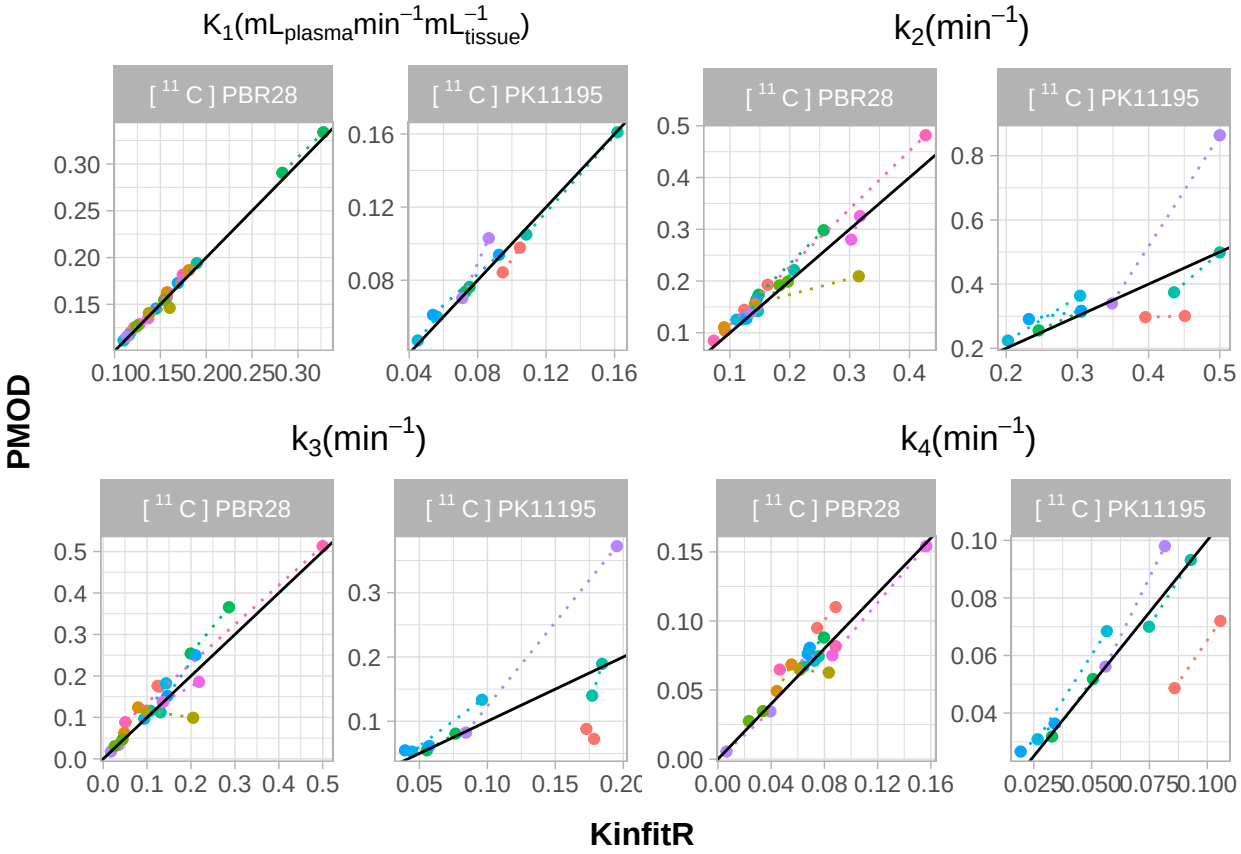
```
#
# ggsave(filename = "micro_ref.png", plot = micro_reference, width = 170, height = 225, units = "mm", d
```

Fig 3, microparameter dotplot with abline for 2tcm

Using the Thalamus ROI

```
K1 <- micro_aif %>%
  ggplot(aes(x = K1_kinfitr, y = K1_pmod, color = subjnumber)) +
  geom_point() +
  geom_line(aes(group=subjnumber), linetype="dotted") +
  geom_abline(slope = 1, intercept = 0) +
  facet_wrap( ~ Ligand, scales = "free", labeller=label_parsed)+ theme(legend.position = "none")+
  ggtitle(expression(paste (K[1], "(",mL[plasma], min^-1, mL[tissue]^-1, ")", sep = ' ')))+
  theme(plot.title = element_text(hjust = 0.5, size = 11)) +
  theme(axis.title = element_blank())

k2_aif <- micro_aif %>%
  ggplot(aes(x = k2_kinfitr, y = k2_pmod, color = subjnumber)) +
  geom_point() +
  geom_line(aes(group=subjnumber), linetype="dotted") +
  geom_abline(slope = 1, intercept = 0) +
  facet_wrap( ~ Ligand, scales = "free", labeller=label_parsed)+ theme(legend.position = "none") +
  ggtitle(expression(paste (k[2], "(", min^-1, ")", sep = ' ')))+
  theme(plot.title = element_text(hjust = 0.5)) +
  theme(axis.title = element_blank())

k3 <- micro_aif %>%
  ggplot(aes(x = k3_kinfitr, y = k3_pmod, color = subjnumber)) +
  geom_point() +
  geom_line(aes(group=subjnumber), linetype="dotted") +
  geom_abline(slope = 1, intercept = 0) +
  facet_wrap( ~ Ligand, scales = "free", labeller=label_parsed)+ theme(legend.position = "none") +
  ggtitle(expression(paste (k[3], "(", min^-1, ")", sep = ' ')))+
  theme(plot.title = element_text(hjust = 0.5)) +
  theme(axis.title = element_blank())


k4 <- micro_aif %>%
  ggplot(aes(x = k4_kinfitr, y = k4_pmod, color = subjnumber)) +
  geom_point() +
  geom_line(aes(group=subjnumber), linetype="dotted") +
  geom_abline(slope = 1, intercept = 0) +
  facet_wrap( ~ Ligand, scales = "free", labeller=label_parsed)+ theme(legend.position = "none") +
  ggtitle(expression(paste (k[4], "(",  min^-1 , ")", sep = ' ')))+
  theme(plot.title = element_text(hjust = 0.5)) +
  theme(axis.title = element_blank())

plot_ref <- plot_grid(K1, k2_aif, k3, k4)

y.grob <- textGrob("PMOD",
                   gp=gpar(fontface="bold", col="black", fontsize=12), rot=90)

x.grob <- textGrob("KinfitR",
```

```
                    gp=gpar(fontface="bold", col="black", fontsize=12))

grid.arrange(arrangeGrob(plot_ref, left = y.grob, bottom = x.grob))
```



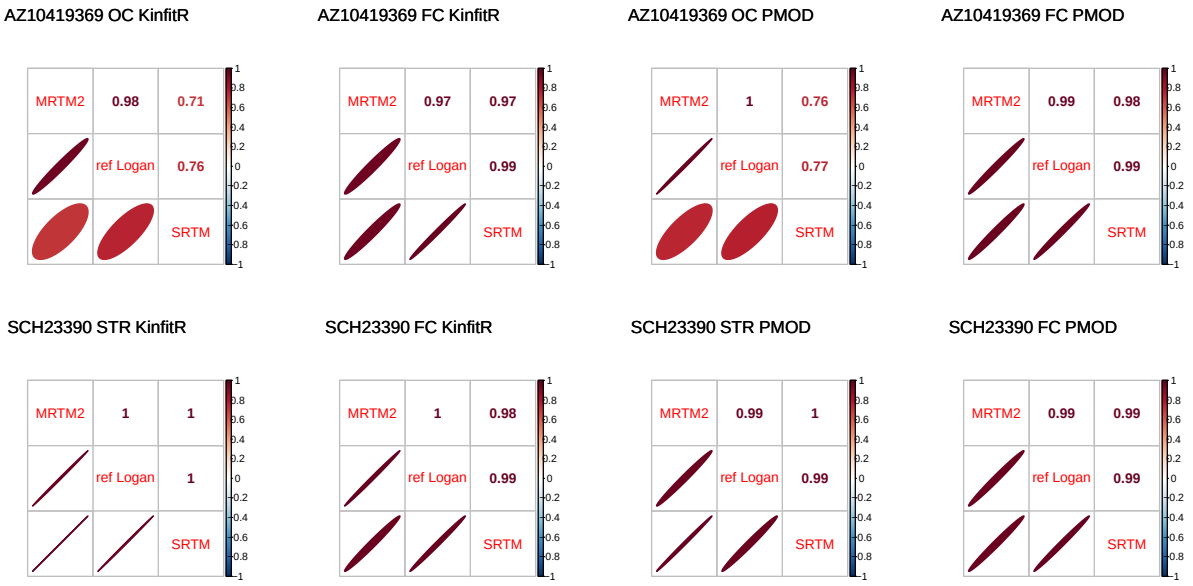

```
#  micro_art <- grid.arrange(arrangeGrob(plot_ref, left = y.grob, bottom = x.grob))
#
# # ggsave(filename = "micro_aif.pdf", plot = micro_art, width = 170, height = 225, units = "mm", dpi =
#
# ggsave(filename = "micro_aif.png", plot = micro_art, width = 170, height = 225, units = "mm", dpi = 3
```

Correlation plots showing the relationship between the different models for the same Ligand.

```
macro <- bind_rows(kinfitr_macro, pmod_macro) %>%
  rename(Ligand = tracer, Model = model) %>%
  mutate(Model = str_replace(string = Model, pattern = "mrtm2", replacement = "MRTM2")) %>%
  mutate(Model = str_replace(string = Model, pattern = "srtm", replacement = "SRTM")) %>% mutate(Model =
  mutate(Model = str_replace(string = Model, pattern = "two_tcm", replacement = "2TCM")) %>% mutate(Mod
  mutate(Model = str_replace(string = Model, pattern = "logan", replacement = "Logan"))

col2 <- colorRampPalette(rev(c("#67001F", "#B2182B", "#D6604D", "#F4A582", "#FDDBC7",
                               "#FFFFFF", "#D1E5F0", "#92C5DE", "#4393C3", "#2166AC", "#053061")))

par(mfrow=c(2,4))

cor_az_oc_kinfitR <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
  spread(Model, Value) %>%
```

```
  filter(Ligand == "az") %>%
  filter(region == "OC") %>%
  filter(software == "kinfitR") %>%
  select(MRTM2:SRTM) %>%
  cor()%>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200),  diag='n',
                 number.digits = 2, title=expression(AZ10419369 ~ OC ~ KinfitR),
                 mar=c(0,0,1,0))

cor_az_fc_kinfitR <- macro %>%
  select(PET, region, Ligand, Model, Value, software) %>%
  spread(Model, Value) %>%
  filter(Ligand == "az") %>%
  filter(region == "FC") %>%
  filter(software == "kinfitR") %>%
  select(MRTM2:SRTM) %>%
  cor() %>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200),  diag='n',
                 number.digits = 2, title=expression(AZ10419369 ~ FC  ~ KinfitR),
                 mar=c(0,0,1,0))

cor_az_oc_pmod <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
  spread(Model, Value) %>%
  filter(Ligand == "az") %>%
  filter(region == "OC") %>%
  filter(software == "pmod") %>%
  select(MRTM2:SRTM) %>%
  cor()%>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200),  diag='n',
                 number.digits = 2, title=expression(AZ10419369 ~ OC ~ PMOD),
                 mar=c(0,0,1,0))

cor_az_fc_pmod <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
  spread(Model, Value) %>%
  filter(Ligand == "az") %>%
  filter(region == "FC") %>%
  filter(software == "pmod") %>%
  select(MRTM2:SRTM) %>%
  cor()%>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200),  diag='n',
                 number.digits = 2, title=expression(AZ10419369 ~ FC  ~ PMOD),
                 mar=c(0,0,1,0))

cor_sch_str_kinfitR <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
  spread(Model, Value) %>%
  filter(Ligand == "sch") %>%
```

```
  filter(region == "STR") %>%
  filter(software == "kinfitR") %>%
  select(MRTM2:SRTM) %>%
  cor()%>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200),  diag='n',
                 number.digits = 2, title=expression(SCH23390 ~ STR ~ KinfitR),
                 mar=c(0,0,1,0))

cor_sch_fc_kinfitR <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
  spread(Model, Value) %>%
  filter(Ligand == "sch") %>%
  filter(region == "FC") %>%
  filter(software == "kinfitR") %>%
  select(MRTM2:SRTM) %>%
  cor()%>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200),  diag='n',
                 number.digits = 2, title=expression(SCH23390 ~ FC ~ KinfitR),
                 mar=c(0,0,1,0))

cor_sch_str_pmod <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
  spread(Model, Value) %>%
  filter(Ligand == "sch") %>%
  filter(region == "STR") %>%
  filter(software == "pmod") %>%
  select(MRTM2:SRTM) %>%
  cor()%>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200),  diag='n',
                 number.digits = 2, title=expression(SCH23390 ~ STR ~ PMOD),
                 mar=c(0,0,1,0))

cor_sch_fc_pmod <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
  spread(Model, Value) %>%
  filter(Ligand == "sch") %>%
  filter(region == "FC") %>%
  filter(software == "pmod") %>%
  select(MRTM2:SRTM) %>%
  cor()%>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200),  diag='n',
                 number.digits = 2, title=expression(SCH23390 ~ FC ~ PMOD),
                 mar=c(0,0,1,0))
```

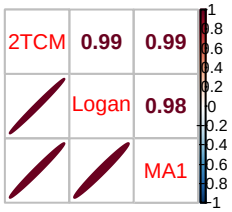



```
par(mfrow=c(2,4))

cor_pk_tha_kinfitR <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
  spread(Model, Value) %>%
  filter(Ligand == "pk") %>%
  filter(region == "THA") %>%
  filter(software == "kinfitR") %>%
  select("2TCM":MA1) %>%
  cor()%>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200),  diag='n',
                 number.digits = 2, title=expression(PK11195 ~ THA ~ KinfitR),
                 mar=c(0,0,1,0))

cor_pk_fc_kinfitR <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
  spread(Model, Value) %>%
  filter(Ligand == "pk") %>%
  filter(region == "FC") %>%
  filter(software == "kinfitR") %>%
  select("2TCM":MA1) %>%
  cor()%>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200),  diag='n',
                 number.digits = 2, title=expression(PK11195 ~ FC ~ KinfitR),
                 mar=c(0,0,1,0))

cor_pk_tha_pmod <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
  spread(Model, Value) %>%
  filter(Ligand == "pk") %>%
  filter(region == "THA") %>%
  filter(software == "pmod") %>%
```

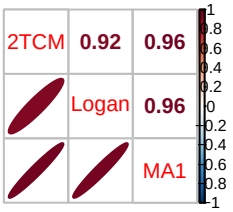
```
  select("2TCM":MA1) %>%
  cor()%>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200),  diag='n',
                 number.digits = 2, title=expression(PK11195 ~ THA ~ pmod),
                 mar=c(0,0,1,0))

cor_pk_fc_pmod <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
  spread(Model, Value) %>%
  filter(Ligand == "pk") %>%
  filter(region == "FC") %>%
  filter(software == "pmod") %>%
  select("2TCM":MA1) %>%
  cor()%>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200),  diag='n',
                 number.digits = 2, title=expression(PK11195 ~ FC ~ pmod),
                 mar=c(0,0,1,0))

cor_pbr28_tha_kinfitR <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
  spread(Model, Value) %>%
  filter(Ligand == "pbr28") %>%
  filter(region == "THA") %>%
  filter(software == "kinfitR") %>%
  select("2TCM":MA1) %>%
  cor()%>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200),  diag='n',
                 number.digits = 2, title=expression(pbr28 ~ THA ~ KinfitR),
                 mar=c(0,0,1,0))

cor_pbr28_fc_kinfitR <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
  spread(Model, Value) %>%
  filter(Ligand == "pbr28") %>%
  filter(region == "FC") %>%
  filter(software == "kinfitR") %>%
  select("2TCM":MA1) %>%
  cor()%>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200),  diag='n',
                 number.digits = 2, title=expression(pbr28 ~ FC ~ KinfitR),
                 mar=c(0,0,1,0))

cor_pbr28_tha_pmod <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
  spread(Model, Value) %>%
  filter(Ligand == "pbr28") %>%
  filter(region == "THA") %>%
  filter(software == "pmod") %>%
  select("2TCM":MA1) %>%
```

```
  cor()%>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200),  diag='n',
                 number.digits = 2, title=expression(pbr28 ~ THA ~ pmod),
                 mar=c(0,0,1,0))

cor_pbr28_fc_pmod <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
  spread(Model, Value) %>%
  filter(Ligand == "pbr28") %>%
  filter(region == "FC") %>%
  filter(software == "pmod") %>%
  select("2TCM":MA1) %>%
  cor()%>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200),  diag='n',
                 number.digits = 2, title=expression(pbr28 ~ FC ~ pmod),
                 mar=c(0,0,1,0))
```

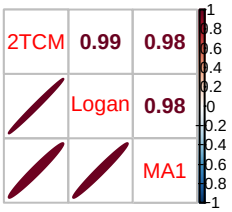
PK11195 THA KinfitR



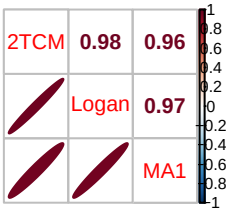
PK11195 FC KinfitR



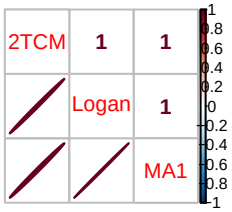
PK11195 THA pmod



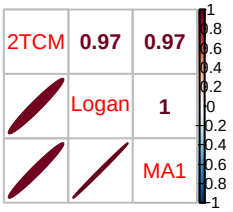
PK11195 FC pmod



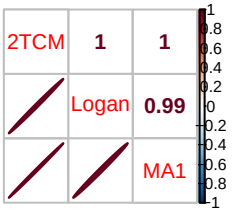
pbr28 THA KinfitR



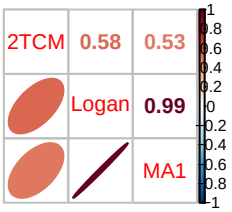
pbr28 FC KinfitR



pbr28 THA pmod



pbr28 FC pmod



#median of the correlations

```
median_invasive_pmod <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
  spread(Model, Value) %>%
  filter(software == "pmod") %>%
  filter(Ligand == "pbr28" | Ligand == "pk") %>%
```

Table 2: Median correlation of the invasive models with PMOD

Median
0.79

Table 3: Median correlation of the invasive models with kinfitr

Median
0.99

```
  select(Ligand:MA1)

median_invasive_pmod %>%
  select(`2TCM`:MA1) %>%
  correlate(quiet = T) %>%
  shave() %>%
  stretch() %>%
  drop_na() %>%
  summarize(Median = median(r)) %>%
  kable(digits = 2, caption = "Median correlation of the invasive models with PMOD")
```

```
median_invasive_kinfitr <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
  spread(Model, Value) %>%
  filter(software == "kinfitR") %>%
  filter(Ligand == "pbr28" | Ligand == "pk") %>%
  select(Ligand:MA1)

median_invasive_kinfitr %>%
  select(`2TCM`:MA1) %>%
  correlate(quiet = T) %>%
  shave() %>%
  stretch() %>%
  drop_na() %>%
  summarize(Median = median(r)) %>%
  kable(digits = 2, caption = "Median correlation of the invasive models with kinfitr")
```

```
median_ref_pmod <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
  spread(Model, Value) %>%
  filter(software == "pmod") %>%
  filter(Ligand == "az" | Ligand == "sch") %>%
  select(MRTM2:SRTM)

median_ref_pmod %>%
  correlate(quiet = T) %>%
  shave() %>%
  stretch() %>%
  drop_na() %>%
  summarize(Median = median(r)) %>%
  kable(digits = 2, caption = "Median correlation of the non-invasive models with PMOD")
```

```
median_ref_kinfitr <- macro %>%
  select(Ligand, PET, region, Model, Value, software) %>%
```

Table 4: Median correlation of the non-invasive models with PMOD

Median
0.99

Table 5: Median correlation of the non-invasive models with kinfitr

Median
0.99

```
  spread(Model, Value) %>%
  filter(software == "kinfitR") %>%
  filter(Ligand == "az" | Ligand == "sch") %>%
  select(MRTM2:SRTM)

median_ref_kinfitr %>%
  correlate(quiet = T) %>%
  shave() %>%
  stretch() %>%
  drop_na() %>%
  summarize(Median = median(r)) %>%
  kable(digits = 2, caption = "Median correlation of the non-invasive models with kinfitr")
```

#microparameter correlations

```
micro_aif %>%
  select(K1_pmod, K1_kinfitr,k2_pmod, k2_kinfitr,k3_pmod, k3_kinfitr,k4_pmod, k4_kinfitr) %>%
  correlate() %>%
  shave() %>%
  stretch() %>%
  filter(!is.na(r))  %>%
  slice(-c(2:13,15:22,24:27)) %>%
  select("Microparameter" = y,r) %>%
  mutate(Microparameter = str_replace_all(string = Microparameter, pattern = "_kinfitr", replacement = "
  kable(digits = 2, caption = "correlation of microparameters between kinfitr and PMOD for the invasive
```

```
micro_ref %>%
  select(R1_pmod,R1_kinfitr,k2_pmod, k2_kinfitr) %>%
  correlate() %>%
  shave() %>%
  stretch() %>%
  filter(!is.na(r)) %>%
  filter(row_number()==1 | row_number()==n()) %>%
  select("Microparameter" = y,r) %>%
  mutate(Microparameter = str_replace_all(string = Microparameter, pattern = "_kinfitr", replacement = "
  kable(digits = 2, caption = "correlation of  microparameters between kinfitr and PMOD for the non_inva
```

\begin{table}[t]

\caption{correlation of microparameters between kinfitr and PMOD for the non_invasive models}

Microparameter	r
R1	1
k2	1

\end{table}

Table 6: correlation of microparameters between kinfitr and PMOD for the invasive models

Microparameter	r
K1	1.00
k2	0.86
k3	0.88
k4	0.90