PK11195

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Aims

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

Libraries

CRAN libraries

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

```
library(tidyverse)
library(stringr)
library(corrplot)
library(grid)
library(gridExtra)
library(RColorBrewer)
library(psych)
library(readxl)
library(pracma)
library(jracma)
library(ime4)
library(rjags)
library(knitr)
library(cowplot)
library(corrplot)
library(ggplotify)
```

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())
```

Creating folders using "initProjectFolder()"

```
initProjectFolder()
```

Extracting roistats and Tidying data.

```
#Extracting tac data
tacs <- tibble(Filename = list.files(path = "../RawData/",</pre>
                                            pattern = "roistats.mat")) %>%
   group by(Filename) %>%
   mutate(tacdata = map(Filename, ~kipettools::roistats_getData(
     paste0("../RawData/", .x))))
tacs <- tacs %>%
  ungroup() %>%
  mutate(Subjname = map_chr(tacdata, "Subjname"),
         PETNo = map_dbl(tacdata, "PETNo"),
         tacdata = map(tacdata, "tacdata")) %>%
  select(-Filename) %>%
  mutate(PET = paste(Subjname, PETNo, sep='_'))
#loading weights and blood data
oldwd <- getwd()</pre>
setwd("../RawData/")
blood <- list()</pre>
bloodfiles <- list.files(pattern='blood_processed_pfhill')</pre>
for(i in 1:length(bloodfiles)) {
blood[[bloodfiles[i]]] <- read_tsv(bloodfiles[i])</pre>
   print(paste0('Progress: ', i, ' / ', length(bloodfiles)))
}
blood <- tibble(blood)</pre>
Weights_list <- list()</pre>
weightfiles <- list.files(pattern='_weights2009')</pre>
for(i in 1:length(weightfiles)) {
Weights_list[[weightfiles[i]]] <- read_csv(weightfiles[i], col_names = FALSE)</pre>
   print(paste0('Progress: ', i, ' / ', length(weightfiles)))
}
setwd(oldwd)
Weights_list <- tibble(Weights_list)</pre>
Weights_list$PET <- weightfiles %>%
str replace(" weights2009.txt", " ")
Weights_list <- Weights_list %>%
group_by(PET) %>%
unnest() %>%
rename(weights = X1) %>%
ungroup()
#Note: new weights added
tacs <- tacs %>%
unnest() %>%
rename(Times = times) %>%
select(Subjname:PET, Times, durations, WM, GM, WB, FC, OC, THA, STR, TC, ACC, CBL = CER, INS) %>%
add_column(weights = Weights_list$weights) %>%
select(-weights) %>%
```

```
mutate("start" = Times - (durations/2)) %>%
mutate("end" = Times + (durations/2))
tacs$weights <- weights_create(t_start = tacs$start, t_end = tacs$end,</pre>
                               tac = tacs$WB, radioisotope = "C11")
tacs <- tacs %>%
group by (PET, Subjname, PETNo) %>%
nest(.key = tacdata) %>%
ungroup()
blood$PET. <- bloodfiles %>%
str_replace("_blood_processed_pfhill.txt", " ")
blood <- blood %>%
  unnest() %>%
rename(Cbl.disp.corr = "Cbl disp corr", Cpl = "Cpl (nCi/cc)", ABSS.sec = "ABSS sec" ) %>%
  mutate(Cbl.disp.corr = ifelse(Cbl.disp.corr < 0, 0, Cbl.disp.corr)) %%</pre>
  group_by(PET.) %>%
  nest(.key='blooddata') %>%
  ungroup() %>%
   mutate(input = map(blooddata, ~blood_interp(
             t_blood = .x$ABSS.sec/60, blood =.x$Cbl.disp.corr,
             t_plasma=.x$ABSS.sec/60, plasma =.x$Cpl,
             t_parentfrac = .x$ABSS.sec/60 , parentfrac= .x$parent_fract ) ))
tacs <- tacs %>%
  arrange(PET, Subjname, PETNo) %>%
  bind_cols(blood)%>%
  select(-PET.)
saveRDS(tacs, '../DerivedData/tacs.rds')
```

Fitting of the Delay and Blood Volume Fraction

$creating \ logan_tstar$

```
logantstar <- function(tacdata, input, inpshift) {
  Logan_tstar(t_tac = tacdata$Times, input = input, lowroi = tacdata$FC, medroi = tacdata$CBL, highro
}
tacs <- tacs %>%
  group_by(Subjname, PETNo) %>%
  mutate(logan_tstar = pmap(list(tacdata, input, inpshift), logantstar))
```

#Rearrangement of the Data into Long Format

```
tacs_long <- tacs %>%
  select(PET, Subjname, PETNo, tacdata, logan_tstar, inpshift) %>%
  unnest(tacdata, .drop = FALSE) %>%
  gather(Region, TAC, -(PET:durations) , -(start:weights)) %>%
  group_by(PET, Subjname, PETNo, Region) %>%
  nest(.key = 'tacdata')

tacs_long <- tacs %>%
  select(PET, Subjname, PETNo, input, delayFit) %>%
  inner_join(tacs_long, by = c("PET", "Subjname", "PETNo"))
```

Plotting logan_tstar

```
set.seed(123)
tstar_fits <- tacs_long %>%
  ungroup() %>%
  select(tacdata, PET) %>%
  unnest() %>%
  select(PET, logan_tstar) %>%
  select(PET, logan_tstar) %>%
  sample_n(size = 4, replace = F)
walk2(list(tstar_fits$logan_tstar), tstar_fits$PET,
    ~print(plot_grid(plotlist = .x, ncol = 1, nrow = 1, labels = paste('PET:',.y), label_x = 0.5, label
```

All 4 tstar plots on a single page

```
plot_grid(plotlist = tstar_fits$logan_tstar, ncol = 2, nrow = 1, labels = paste('PET:',tstar_fits$PET),
    draw_figure_label("t*", position = "top", fontface = "bold", size = 32, colour = "red")
```

Define functions for fitting the models

Comment: when the argumant "multstart_iter" is equal to 1 for 2TCM, the estimated microparameters of a number of study participants have a tendency of approaching or even exceeding their default limits.

Fit kinetic models

#Plot kinetic models

Plot 2tcm

```
delayFits <- map(tacs_long$delayFit[tacs_long$Region=='WB'],</pre>
                ~plot_inptac_fit(.x) + ggtitle('Delay'))
delayFits <- data.frame(PET = unique(tacs_long$PET)) %>%
              mutate(fit = delayFits)
plot_2tcm <- tacs_long %>%
group_by(PET, Region) %>%
  mutate(fit = map2(fit_2tcm, Region,
      ~ plot_kinfit(.x, roiname = .y))) %>%
  ungroup() %>%
  filter(Region %in% c('FC', 'WB', 'ACC', 'CBL', 'THA')) %>%
  select(PET, fit) %>%
  group_by(PET) %>%
  arrange(PET) %>%
  bind_rows(delayFits)
walk2(list(plot_2tcm\fit), unique(plot_2tcm\fit),
    ~print(plot_grid( plotlist = .x, ncol = 2, nrow = 3, align = 'hv') +
  draw_plot_label( label = .y , y = 1, x = 0.5, fontface = "bold", size = 20, colour = "red", hjust = 1
###subplot version
plot.TAC <- plot_kinfit(tacs_long$fit_2tcm[[4]], roiname = tacs_long$Region[4])</pre>
plot.AIF <- plot_kinfit(tacs_long$fit_2tcm[[4]], roiname = tacs_long$Region[4]) +</pre>
coord_cartesian(ylim=c(0,3000))
p <- ggdraw() +
 draw_plot(plot.TAC + theme(legend.position = "none"), 0, 0, 1, 1) +
```

new plot 2tcm

```
k <- tacs_long %>%
group_by(PET, Region) %>%
mutate(twotcm = map(fit_2tcm, c("tacs"))) %>%
select(PET, Region, twotcm) %>%
filter(Region %in% c('FC', 'WB', 'ACC', 'CBL')) %>%
unnest()

ggplot(k, aes(x=Time, y=Target, color = Region)) +
geom_point() + geom_line(aes(y=Target_fitted, color = Region)) +
facet_wrap(~ PET , ncol=2)
```

Plot ma1

Plot Loganplot

```
group_by(PET) %>%
arrange(PET)

walk2(list(plot_Logan$fit), unique(plot_Logan$PET),
    ~print(plot_grid( plotlist = .x, ncol = 2, nrow = 2, align = 'hv') +
draw_plot_label( label = .y , y = 1, x = 0.5, fontface = "bold", size = 20, colour = "red", hjust = 1
```

Test-retest

trt preparation

```
trt_check <- tacs_long %>%
  select(Subjname, PETNo, Region, Vt_ma1, Vt_2tcm, Vt_Logan) %>%
  gather(Measure, Value, -Subjname, -PETNo, -Region) %>%
  group_by(Region, Measure) %>%
  nest(.key = "data")

# saveRDS(tacs_long,'../DerivedData/raw_kinfit_pk11195.rds')
```

trt results

Region	Measure	mean	sd	cov	skew	kurtosis	icc	icc_l	icc_u	wscv	sdd	absvar	signv
WM	Vt_ma1	0.850	0.213	0.251	0.121	-1.703	0.708	0.031	0.951	0.142	0.335	0.129	-0.10
GM	Vt_ma1	0.794	0.178	0.224	0.170	-1.546	0.675	-0.078	0.946	0.132	0.291	0.150	-0.04
WB	Vt_ma1	0.802	0.185	0.231	0.175	-1.557	0.666	-0.095	0.944	0.137	0.306	0.156	-0.04
FC	Vt_ma1	0.785	0.162	0.206	0.176	-1.560	0.652	-0.120	0.941	0.125	0.273	0.148	-0.04
OC	Vt_ma1	0.849	0.200	0.236	0.069	-1.596	0.683	-0.063	0.947	0.137	0.323	0.153	-0.04
THA	Vt_ma1	0.836	0.220	0.264	0.405	-1.180	0.731	0.034	0.956	0.141	0.328	0.179	-0.04
STR	Vt_ma1	0.793	0.167	0.211	0.281	-0.736	0.584	-0.228	0.928	0.140	0.308	0.154	0.07
TC	Vt_ma1	0.784	0.179	0.229	0.061	-1.643	0.660	-0.105	0.943	0.138	0.299	0.156	-0.04
ACC	Vt_ma1	0.760	0.180	0.236	0.436	-1.122	0.569	-0.250	0.924	0.160	0.337	0.212	-0.09
CBL	Vt_ma1	0.797	0.199	0.250	0.095	-1.602	0.696	-0.038	0.950	0.142	0.314	0.151	-0.0
INS	Vt_ma1	0.776	0.193	0.249	0.217	-1.647	0.621	-0.171	0.935	0.158	0.340	0.169	-0.07
WM	Vt_2tcm	14.879	23.778	1.598	1.013	-1.024	0.637	-0.146	0.938	0.993	40.932	0.445	-0.33
GM	Vt_2tcm	0.683	0.156	0.228	0.472	-0.799	0.749	0.075	0.960	0.118	0.224	0.156	0.00
WB	Vt_2tcm	0.725	0.155	0.214	0.231	-1.333	0.734	0.039	0.957	0.115	0.230	0.145	-0.02
FC	Vt_2tcm	0.689	0.141	0.205	0.369	-1.072	0.711	-0.007	0.953	0.115	0.220	0.152	-0.00
OC	Vt_2tcm	0.728	0.168	0.230	0.308	-1.002	0.731	0.033	0.956	0.124	0.249	0.168	0.0

Region	Measure	mean	sd	cov	skew	kurtosis	icc	icc_l	icc_u	wscv	sdd	absvar	signv
THA	Vt_2tcm	0.760	0.206	0.271	0.689	-0.601	0.753	0.083	0.960	0.139	0.294	0.189	-0.01
STR	Vt_2tcm	0.761	0.180	0.237	0.541	-0.796	0.132	-0.672	0.804	0.222	0.468	0.248	0.07
TC	Vt_2tcm	0.673	0.149	0.221	0.320	-1.035	0.715	0.001	0.954	0.122	0.228	0.159	0.00
ACC	Vt_2tcm	0.670	0.162	0.242	0.812	-0.320	0.643	-0.135	0.940	0.149	0.277	0.175	-0.03
CBL	Vt_2tcm	0.689	0.170	0.247	0.529	-0.992	0.617	-0.178	0.934	0.157	0.300	0.175	-0.0
INS	Vt_2tcm	0.664	0.173	0.260	0.694	-0.586	0.792	0.178	0.967	0.123	0.227	0.154	0.00
WM	Vt_Logan	0.720	0.191	0.265	0.097	-1.620	0.659	-0.089	0.943	0.160	0.319	0.174	-0.08
GM	Vt_Logan	0.691	0.164	0.238	0.483	-1.010	0.753	0.084	0.960	0.122	0.234	0.151	-0.03
WB	Vt_Logan	0.688	0.168	0.245	0.407	-1.104	0.730	0.032	0.956	0.131	0.251	0.163	-0.04
FC	Vt_Logan	0.673	0.152	0.226	0.525	-0.937	0.728	0.028	0.956	0.122	0.227	0.152	-0.04
OC	Vt_Logan	0.730	0.177	0.242	0.341	-1.155	0.752	0.080	0.960	0.125	0.253	0.153	-0.03
THA	Vt_Logan	0.764	0.208	0.272	0.645	-0.741	0.795	0.186	0.968	0.129	0.273	0.172	-0.01
STR	Vt_Logan	0.674	0.160	0.238	0.674	-0.299	0.683	-0.062	0.948	0.138	0.258	0.149	0.00
TC	Vt_Logan	0.679	0.157	0.231	0.380	-1.183	0.762	0.105	0.962	0.117	0.220	0.144	-0.0
ACC	Vt_Logan	0.682	0.172	0.252	0.515	-0.851	0.631	-0.154	0.937	0.157	0.297	0.204	-0.0
CBL	Vt_Logan	0.701	0.168	0.239	0.553	-0.850	0.738	0.049	0.958	0.127	0.246	0.152	-0.0
INS	Vt_Logan	0.690	0.179	0.259	0.489	-1.032	0.781	0.151	0.965	0.126	0.241	0.154	-0.0

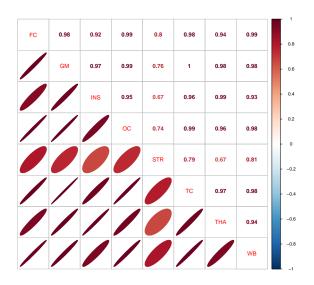
Interregional Correlation

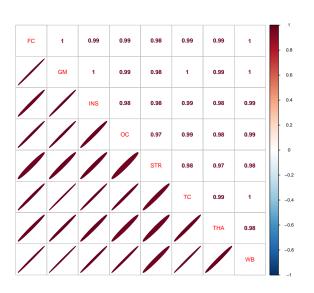
Here the interregional correlations for V_T are assessed

```
Vt_2TCM <- tacs_long %>%
  ungroup() %>%
  select(PET, Region, Vt_2tcm) %>%
  spread(Region, Vt_2tcm)
Vt_MA1 <- tacs_long %>%
  ungroup() %>%
  select(PET, Region, Vt_ma1) %>%
  spread(Region, Vt_ma1)
Vt_logan <- tacs_long %>%
  ungroup() %>%
  select(PET, Region, Vt_Logan) %>%
  spread(Region, Vt_Logan)
col2 <- colorRampPalette(rev(c("#67001F", "#B2182B", "#D6604D", "#F4A582", "#FDDBC7",</pre>
                           "#FFFFFF", "#D1E5F0", "#92C5DE", "#4393C3", "#2166AC", "#053061")))
par(mfrow=c(2,2))
Vt_2TCM %>%
  select(FC:WB) %>%
  cor() %>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200), diag='n',
                 number.digits = 2, title=expression(Vt_2TCM ~ Correlations),
                 mar=c(0,0,1,0)
Vt_logan %>%
 select(FC:WB) %>%
```

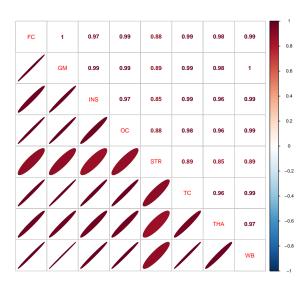
Vt_2TCM Correlations

Vt_logan Correlations





Vt_MA1 Correlations

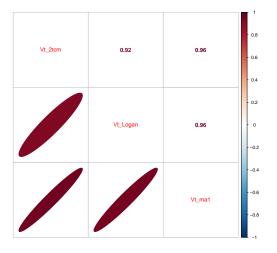


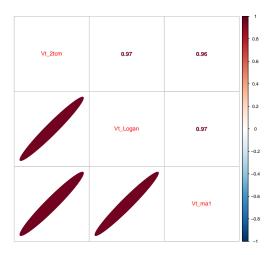
#Corrplot between measures for a single region

```
compare <- tacs_long %>%
  ungroup() %>%
  select(PET, Region, Vt_2tcm, Vt_Logan ,Vt_ma1 ) %>%
  filter(Region %in% c('FC', 'WB', 'STR', 'OC'))
par(mfrow=c(2,2))
compare %>%
  filter(Region == "FC") %>%
  select(Vt_2tcm:Vt_ma1) %>%
  cor() %>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200), diag='n',
                 number.digits = 2, title=expression(Model ~ Correlations ~ Region: FC),
                 mar=c(0,0,1,0)
compare %>%
  filter(Region == "OC") %>%
  select(Vt_2tcm:Vt_ma1) %>%
  cor() %>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200), diag='n',
                 number.digits = 2, title=expression(Model ~ Correlations ~ Region: OC),
                 mar=c(0,0,1,0)
compare %>%
  filter(Region == "STR") %>%
  select(Vt_2tcm:Vt_ma1) %>%
  cor() %>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200), diag='n',
                 number.digits = 2, title=expression(Model ~ Correlations ~ Region: STR),
                 mar=c(0,0,1,0)
compare %>%
  filter(Region == "WB") %>%
  select(Vt_2tcm:Vt_ma1) %>%
  cor() %>%
  corrplot.mixed(lower='ellipse', upper='number',
                 lower.col = col2(200), upper.col = col2(200), diag='n',
                 number.digits = 2, title=expression(Model ~ Correlations ~ Region: WB),
                 mar=c(0,0,1,0)
```



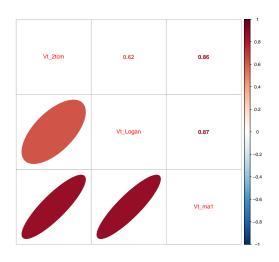
Model Correlations Region : OC

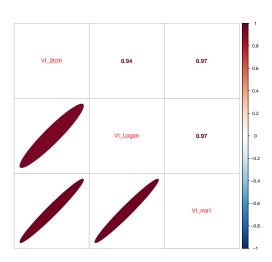




Model Correlations Region : STR

Model Correlations Region : WB





Vt corellation

R-squared

```
trtdata <- tacs_long %>%
    select(PET, Subjname, PETNo, Region, Vt_2tcm, Vt_Logan ,Vt_ma1) %>%
    gather(Measure, Value, -(PET:Region)) %>%
    spread(Region, Value)

trtdata <- trtdata %>%
    gather(Region, Value, -(PET:Measure)) %>%
    unite(Outcome, Measure, Region) %>%
    spread(Outcome, Value)
```

```
corout <- trtdata %>%
  gather(Measure, Binding, -(PET:PETNo), -Vt_2tcm_WB) %>%
  group by(Measure) %>%
  summarise('R^2'=cor(Binding, Vt 2tcm WB)^2) %>%
  arrange(Measure) %>%
  ungroup() %>%
  mutate(Measure = str_replace(string=Measure, pattern='_', replacement='~')) %>%
  mutate(Measure = str replace(string=Measure, pattern='FC', replacement='FC')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='CBL', replacement='CBL~')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='ACC', replacement='ACC')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='INS', replacement='INS')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='THA', replacement='THA')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='WB', replacement='WB~')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='0C', replacement='0C~')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='WM', replacement='WM~')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='GM', replacement='GM-')) %>%
  mutate(Measure = str_replace(string=Measure, pattern='STR', replacement='STR'))
kable(corout, digits=2, caption="Correlations with BP_srtm~WB~")
```

Table 2: Correlations with BP_srtm_{WB}

Measure	R^2
$\overline{\mathrm{Vt}_{\mathrm{2tcm_ACC}}}$	0.86
Vt_{2tcm_CBL}	0.94
${ m Vt}_{ m 2tcm_FC}$	0.98
Vt_{2tcm_GM}	0.96
${ m Vt}_{ m 2tcm_INS}$	0.87
Vt_{2tcm_OC}	0.96
Vt_{2tcm_STR}	0.66
$Vt{\sim}2tcm_TC$	0.97
$\rm Vt_{2tcm_THA}$	0.88
Vt_{2tcm_WM}	0.52
Vt_{Logan_ACC}	0.81
$Vt_{\rm Logan_CBL}$	0.87
Vt_{Logan_FC}	0.87
Vt_{Logan_GM}	0.87
Vt_{Logan_INS}	0.86
Vt_{Logan_OC}	0.91
Vt_{Logan_STR}	0.80
$Vt\sim Logan_TC$	0.88
Vt_{Logan_THA}	0.81
Vt_{Logan_WB}	0.89
Vt_{Logan_WM}	0.88
${ m Vt_{ma1_ACC}}$	0.85
${\rm Vt_{ma1_CBL}}$	0.95
${ m Vt_{ma1_FC}}$	0.96
${ m Vt_{ma1_GM}}$	0.95
${ m Vt_{ma1_INS}}$	0.89
Vt_{ma1} _OC	0.94
Vt_{ma1_STR}	0.84
$Vt\sim ma1_TC$	0.94
$\rm Vt_{ma1_THA}$	0.90

Measure	\mathbb{R}^2			
	$0.95 \\ 0.86$			

#Plot of the change between PETNo = 1 and PETNo = 2.

#all estimates in all models using facet grid.

```
trt_table_2tcm <- trt_table %>%
  gather(estimate, Value, -(Region:Measure))

ggplot(trt_table_2tcm, aes(y = Region, x = Value, colour = Region ))+
  geom_point()+
  facet_grid( Measure ~ estimate)+
  coord_flip()
```

###All estimates in all models using facet_wrap, improved version?

```
trt_table_2TCM <- trt_table %%
  gather(estimate, Value, -(Region:mean)) %>%
  filter(estimate %in% c('icc', 'wscv', 'sd', 'cov'))

ggplot(trt_table_2TCM, aes(y = estimate, x = Value, colour = Region ))+
  geom_point()+
  facet_wrap( ~ Measure)+
  coord_flip()+
  xlim( 0, 1.25)
```

#Old version ma1 plot

Kept in case we would require this code in the future

```
bind_rows(DelayFits) %>%
   arrange(PET, Plot)

allFits_ma1_excluded <- allfits_2tcm %>%
   filter(grepl(PET, pattern='uqis_2'))

allfits_ma1 <- allfits_ma1 %>%
   filter(!grepl(PET, pattern='uqis_2'))

fitLabels <- unique(allfits_ma1$PET)
marrangeGrob(allfits_ma1$Fit, nrow=2, ncol=3, top=quote(paste('PET: ', PETs[g])))</pre>
```