

THE UTILITY OF MIXED-EFFECT MODELS IN THE EVALUATION OF COMPLEX GENOMIC TRAITS IN-VITRO

Supplementary Data: Diagnostic Plots
(with Code)

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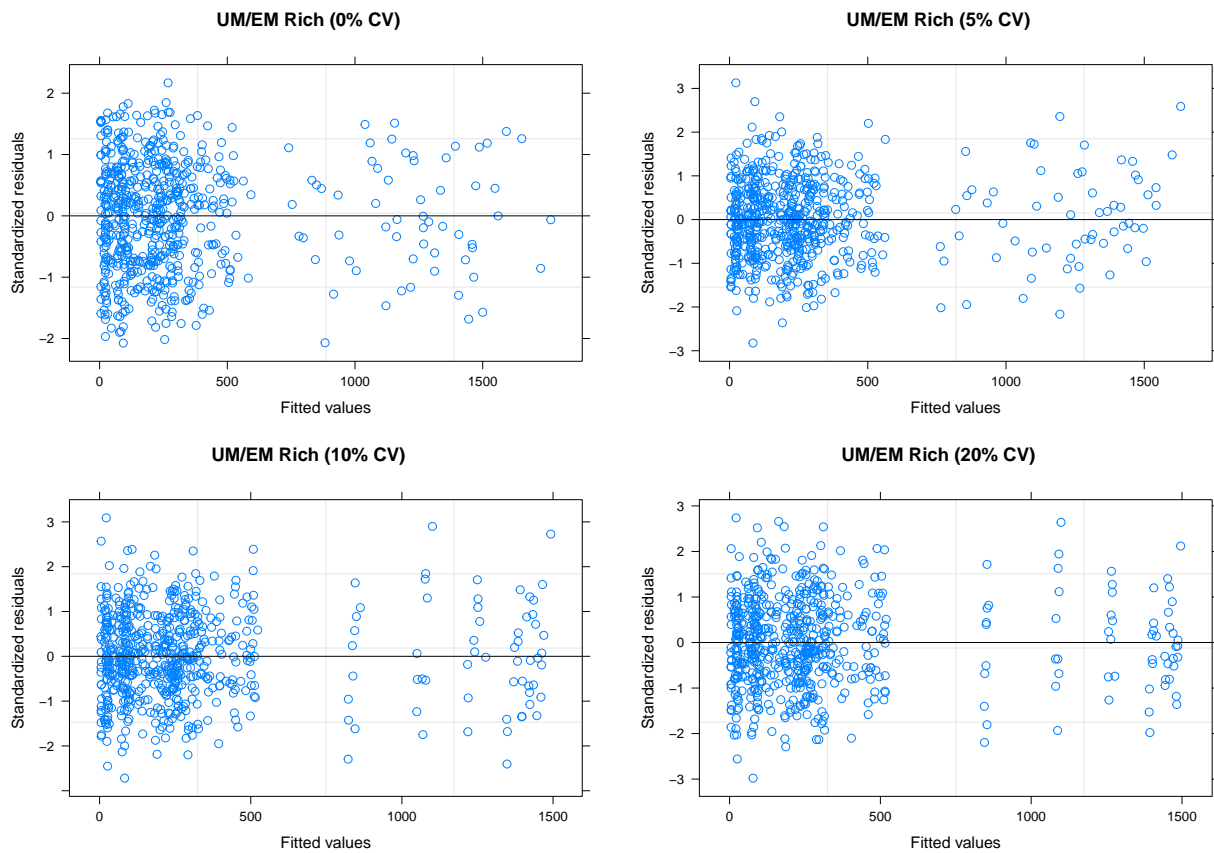
Data Availability:

R Scripts and data necessary to reproduce our analysis are available and can be cloned using the following public repository. (<http://nathanalade.github.io/In-Vitro-NLME/>)

Final Model Residual Plots (UM/EM)

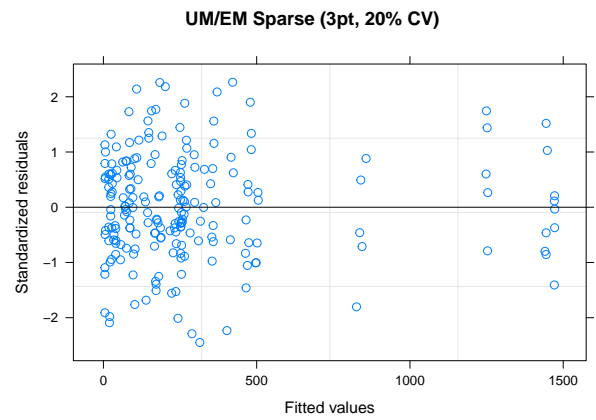
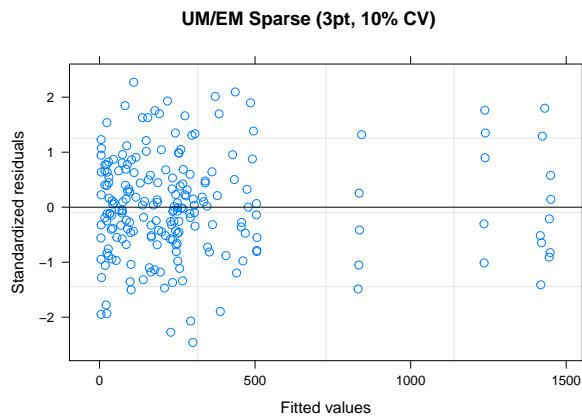
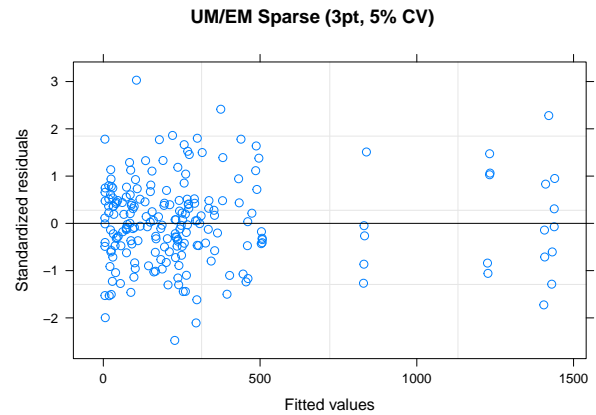
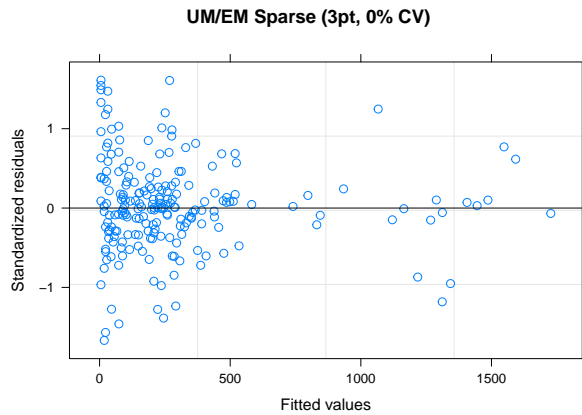
Rich Study Designs (0-20% CV)

```
par(mfrow = c(1, 2))
plot(rich_covar.nlme, main = "UM/EM Rich (0% CV)")
plot(rich_CV5_covar.nlme, main = "UM/EM Rich (5% CV)")
plot(rich_CV10_covar.nlme, main = "UM/EM Rich (10% CV)")
plot(rich_CV20_covar.nlme, main = "UM/EM Rich (20% CV)")
```



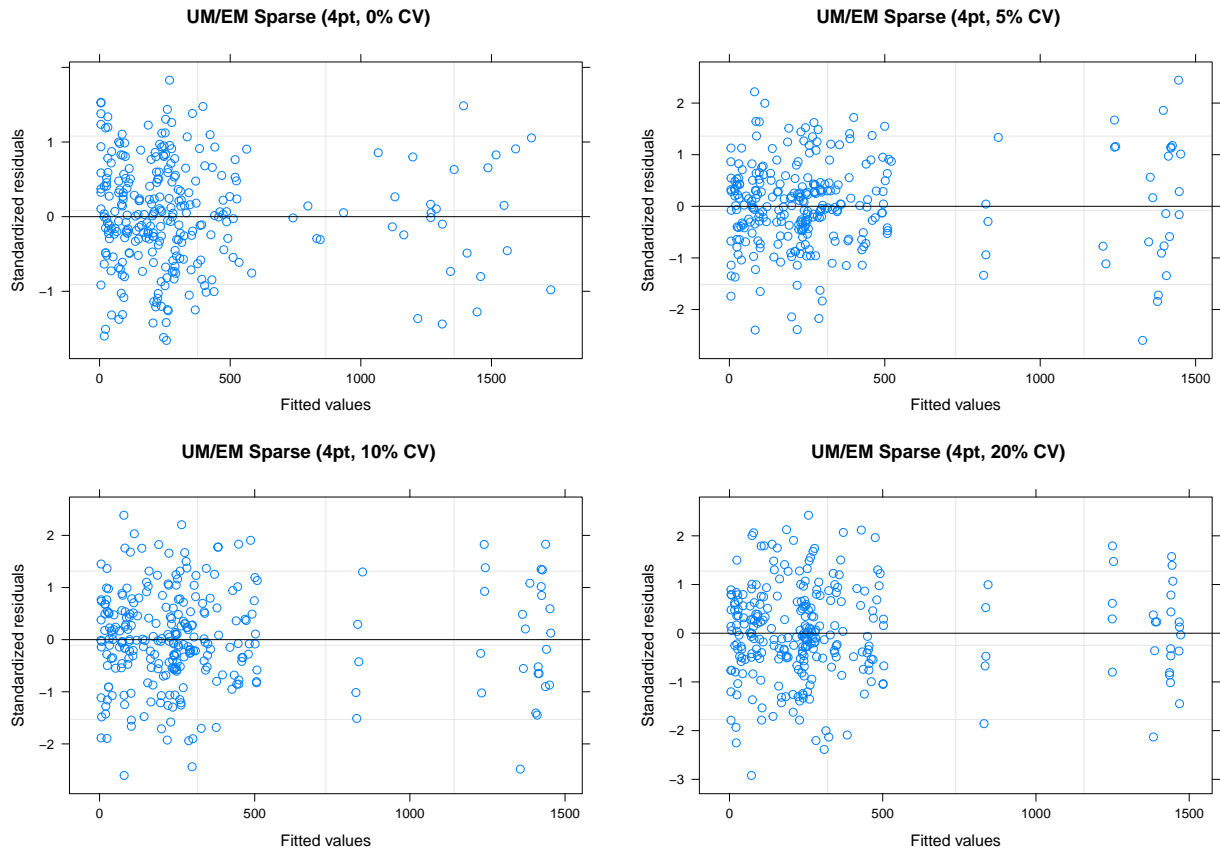
Sparse Study Designs (3pt, 0-20% CV)

```
par(mfrow = c(1, 2))
plot(sparse3pt_covar.nlme, main = "UM/EM Sparse (3pt, 0% CV)")
plot(sparse3pt_CV5_covar.nlme, main = "UM/EM Sparse (3pt, 5% CV)")
plot(sparse3pt_CV10_covar.nlme, main = "UM/EM Sparse (3pt, 10% CV)")
plot(sparse3pt_CV20_covar.nlme, main = "UM/EM Sparse (3pt, 20% CV)")
```



Sparse Study Designs (4pt, 0-20% CV)

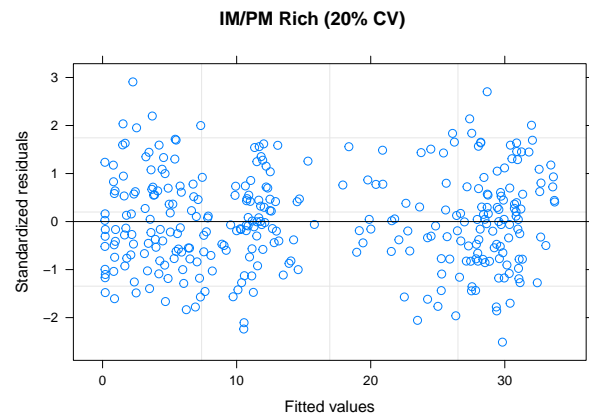
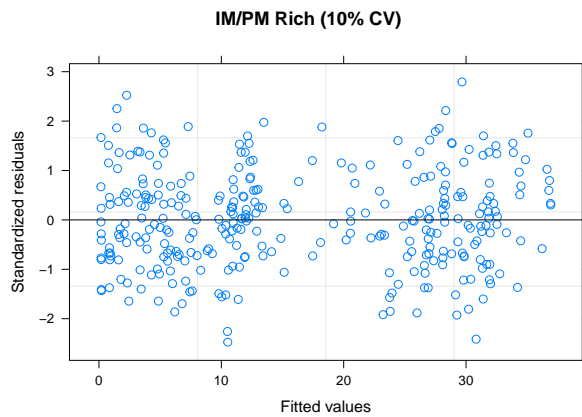
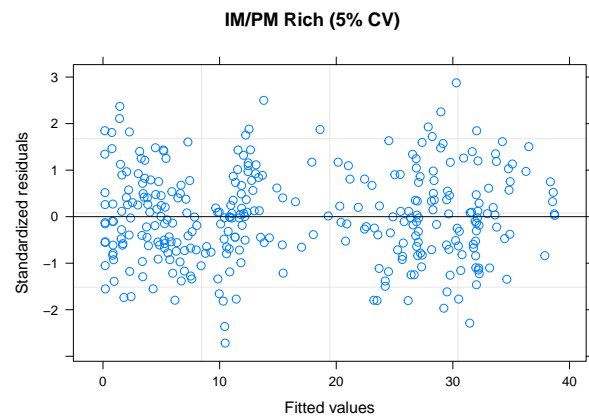
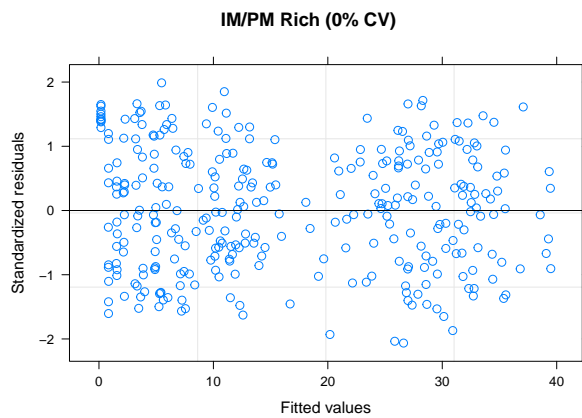
```
par(mfrow = c(1, 2))  
plot(sparse4pt_covar.nlme, main = "UM/EM Sparse (4pt, 0% CV)")  
plot(sparse4pt_CV5_covar.nlme, main = "UM/EM Sparse (4pt, 5% CV)")  
plot(sparse4pt_CV10_covar.nlme, main = "UM/EM Sparse (4pt, 10% CV)")  
plot(sparse4pt_CV20_covar.nlme, main = "UM/EM Sparse (4pt, 20% CV)")
```



Final Model Residual Plots (IM/PM)

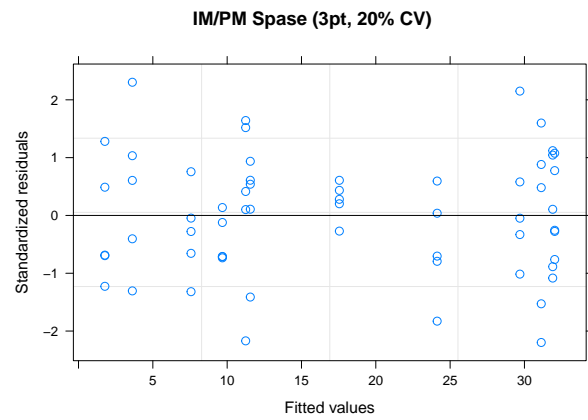
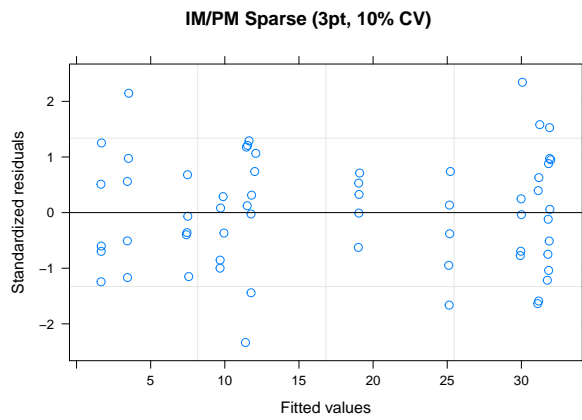
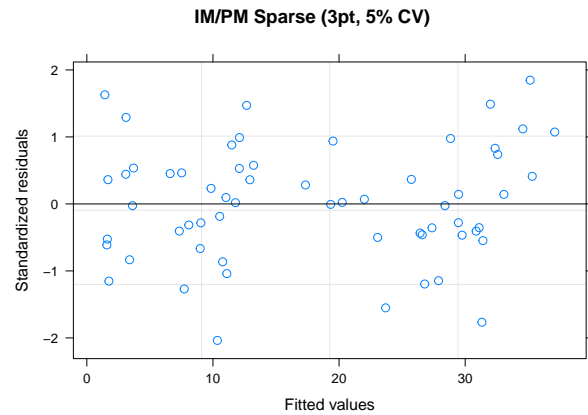
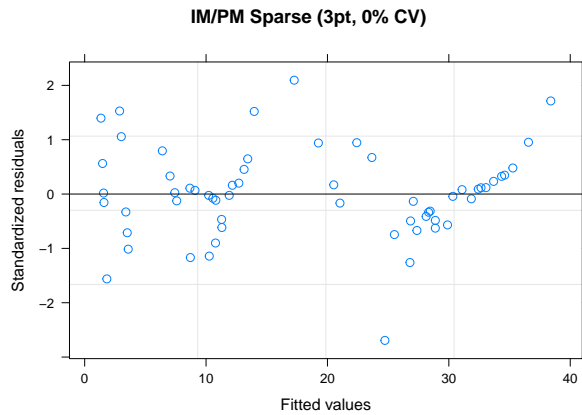
Rich Study Designs (IM/PM, 0-20% CV)

```
par(mfrow = c(1, 2))
plot(PM_covar.nlme, main = "IM/PM Rich (0% CV)")
plot(PM_CV5_covar.nlme, main = "IM/PM Rich (5% CV)")
plot(PM_CV10_covar.nlme, main = "IM/PM Rich (10% CV)")
plot(PM_CV20_covar.nlme, main = "IM/PM Rich (20% CV)")
```



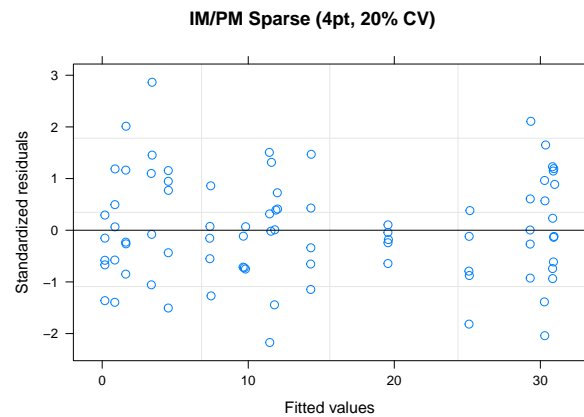
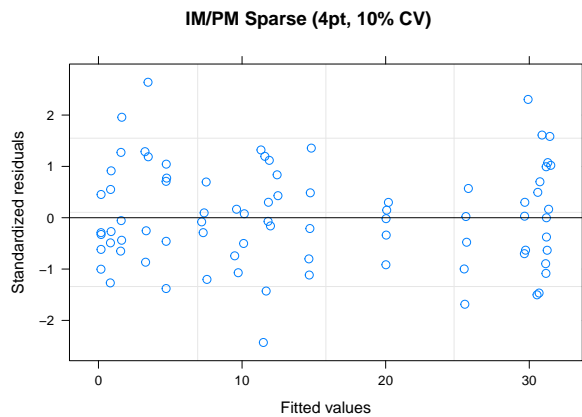
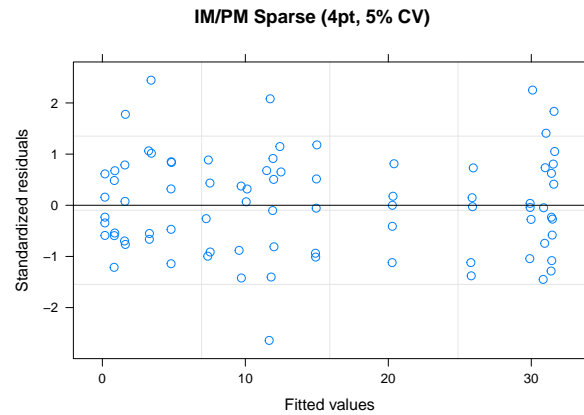
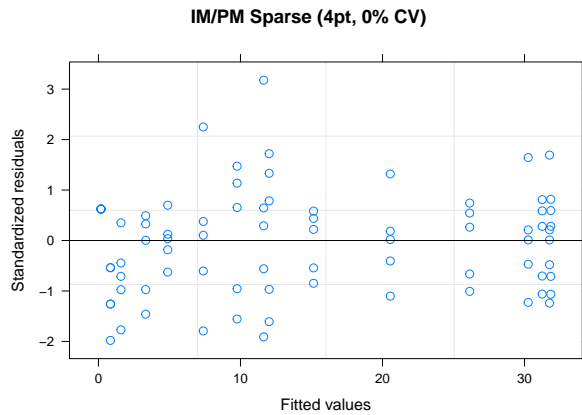
Sparse Study Designs (IM/PM, 3pt, 0-20% CV)

```
par(mfrow = c(1, 2))
plot(PM_3pt_covar.nlme, main = "IM/PM Sparse (3pt, 0% CV)")
plot(PM_3pt_CV5_covar.nlme, main = "IM/PM Sparse (3pt, 5% CV)")
plot(PM_3pt_CV10_covar.nlme, main = "IM/PM Sparse (3pt, 10% CV)")
plot(PM_3pt_CV20_covar.nlme, main = "IM/PM Sparse (3pt, 20% CV)")
```



Sparse Study Designs (IM/PM, 4pt, 0-20% CV)

```
par(mfrow = c(1, 2))  
plot(PM_4pt_covar.nlme, main = "IM/PM Sparse (4pt, 0% CV)")  
plot(PM_4pt_CV5_covar.nlme, main = "IM/PM Sparse (4pt, 5% CV)")  
plot(PM_4pt_CV10_covar.nlme, main = "IM/PM Sparse (4pt, 10% CV)")  
plot(PM_4pt_CV20_covar.nlme, main = "IM/PM Sparse (4pt, 20% CV)")
```



Predicted vs Observed Plots by CYP2D6 Genotype (UM/EM)

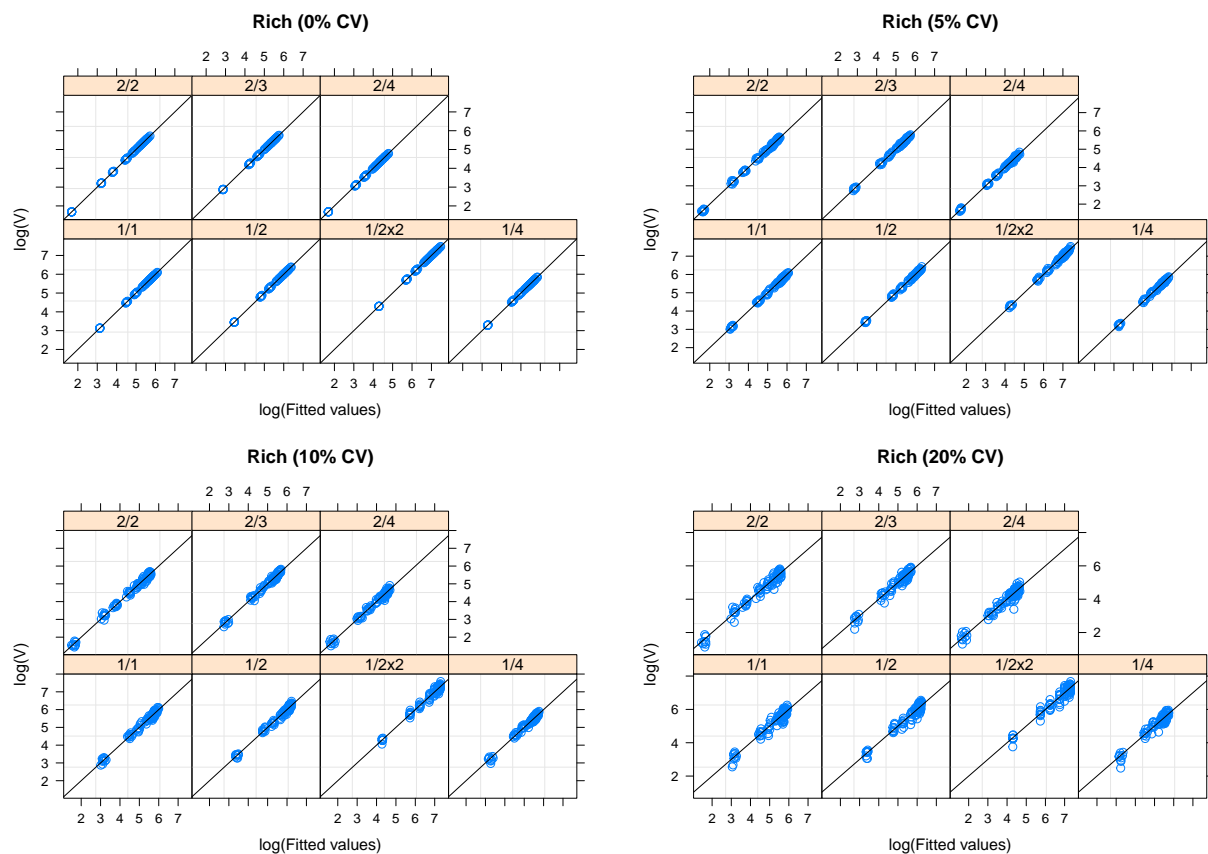
Rich Study Designs

```
par(mfrow = c(1, 2))
plot(rich_covar.nlm, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), main = "Rich (0% CV)",
     xlab = "log(Fitted values)")

plot(rich_CV5_covar.nlm, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), main = "Rich (5% CV)",
     xlab = "log(Fitted values)")

plot(rich_CV10_covar.nlm, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), main = "Rich (10% CV)",
     xlab = "log(Fitted values)")

plot(rich_CV20_covar.nlm, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), main = "Rich (20% CV)",
     xlab = "log(Fitted values)")
```



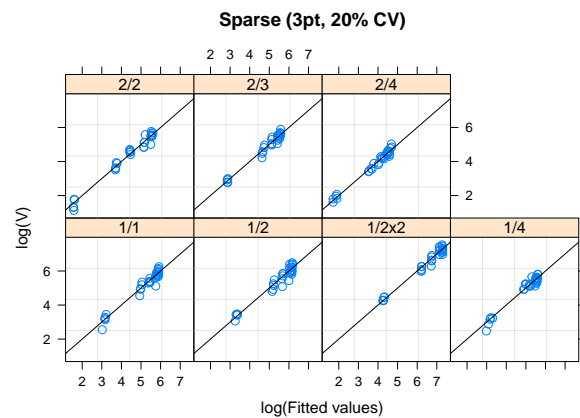
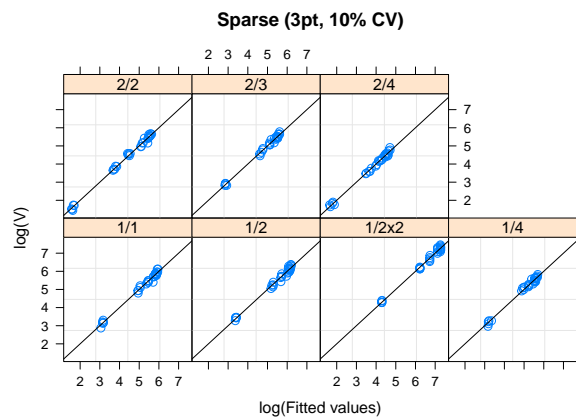
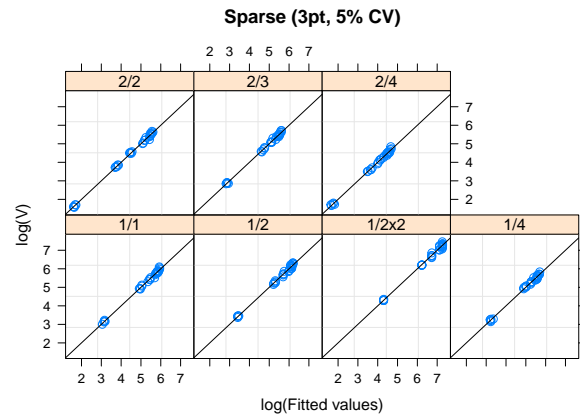
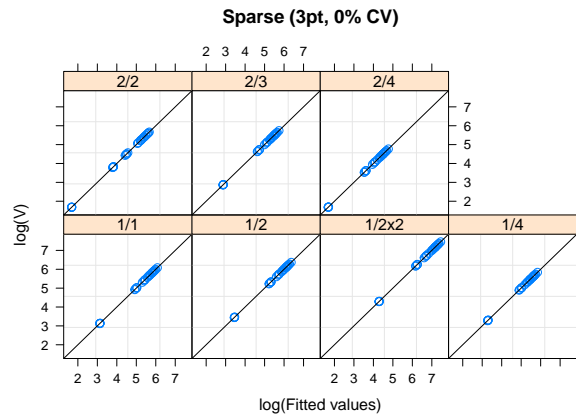
Sparse Study Designs (3pt)

```
par(mfrow = c(1, 2))
plot(sparse3pt_covar.nlme, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), main = "Sparse (3pt, 0% CV)",
     xlab = "log(Fitted values)")

plot(sparse3pt_CV5_covar.nlme, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), main = "Sparse (3pt, 5% CV)",
     xlab = "log(Fitted values)")

plot(sparse3pt_CV10_covar.nlme, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), main = "Sparse (3pt, 10% CV)",
     xlab = "log(Fitted values)")

plot(sparse3pt_CV20_covar.nlme, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), main = "Sparse (3pt, 20% CV)",
     xlab = "log(Fitted values)")
```



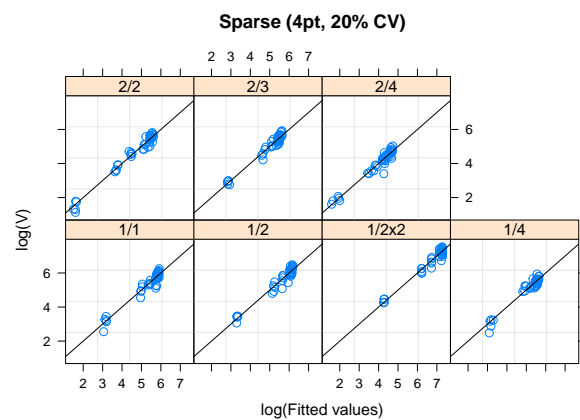
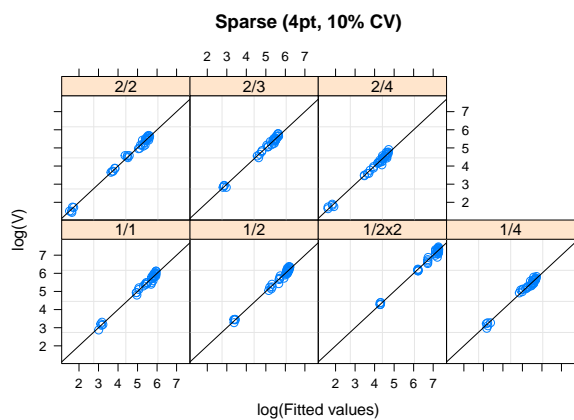
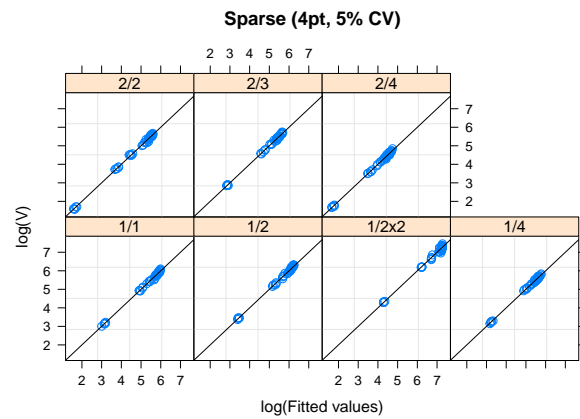
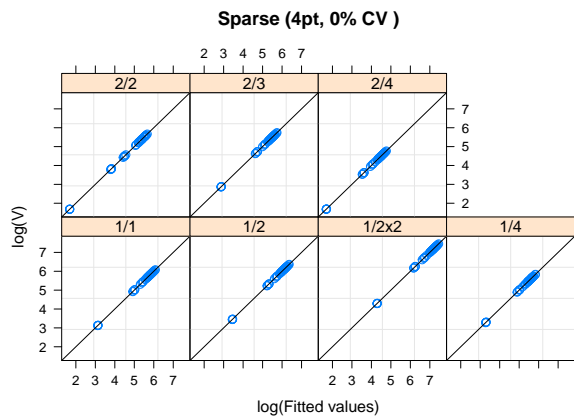
Sparse Study Designs (4pt)

```
par(mfrow = c(1, 2))
plot(sparse4pt_covar.nlme, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), main = "Sparse (4pt, 0% CV )",
     xlab = "log(Fitted values)")

plot(sparse4pt_CV5_covar.nlme, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), main = "Sparse (4pt, 5% CV)",
     xlab = "log(Fitted values)")

plot(sparse4pt_CV10_covar.nlme, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), main = "Sparse (4pt, 10% CV)",
     xlab = "log(Fitted values)")

plot(sparse4pt_CV20_covar.nlme, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), main = "Sparse (4pt, 20% CV)",
     xlab = "log(Fitted values)")
```



Predicted vs Observed Plots by CYP2D6 Genotype (IM/PM)

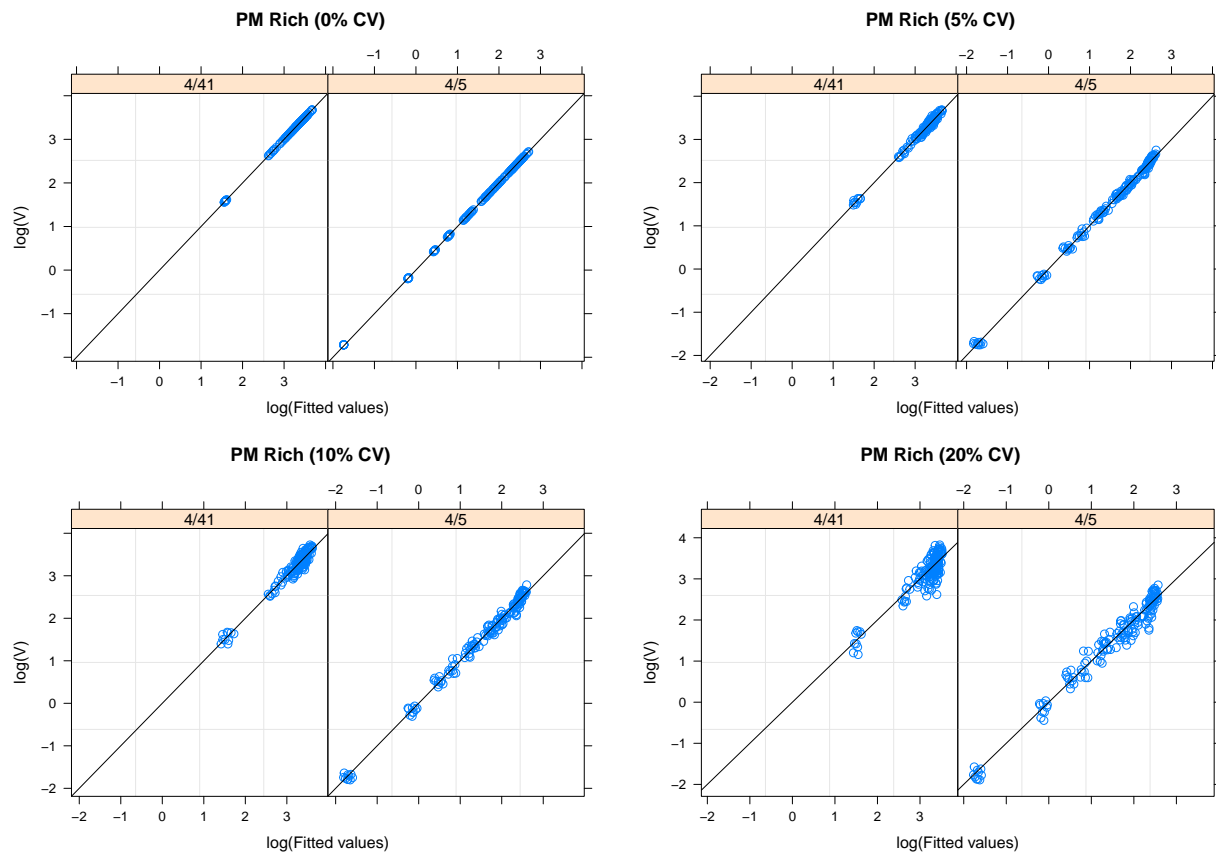
Rich Study Designs

```
par(mfrow = c(1, 2))
plot(PM_covar.nlme, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), xlab = "log(Fitted values)",
     main = "PM Rich (0% CV)")

plot(PM_CV5_covar.nlme, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), xlab = "log(Fitted values)",
     main = "PM Rich (5% CV)")

plot(PM_CV10_covar.nlme, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), xlab = "log(Fitted values)",
     main = "PM Rich (10% CV)")

plot(PM_CV20_covar.nlme, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), xlab = "log(Fitted values)",
     main = "PM Rich (20% CV)")
```



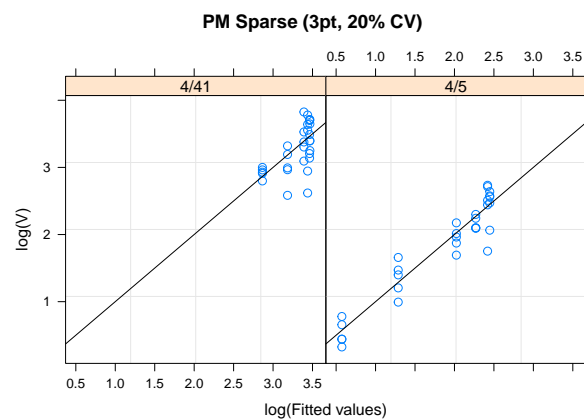
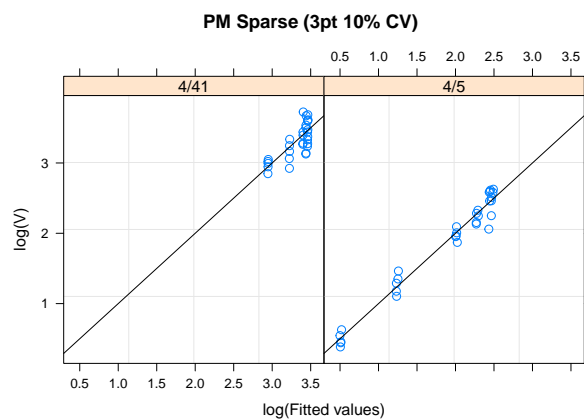
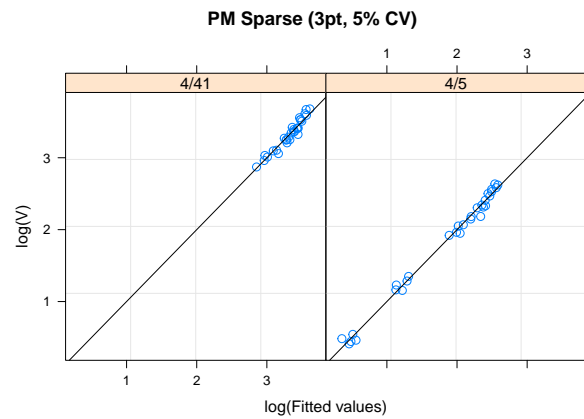
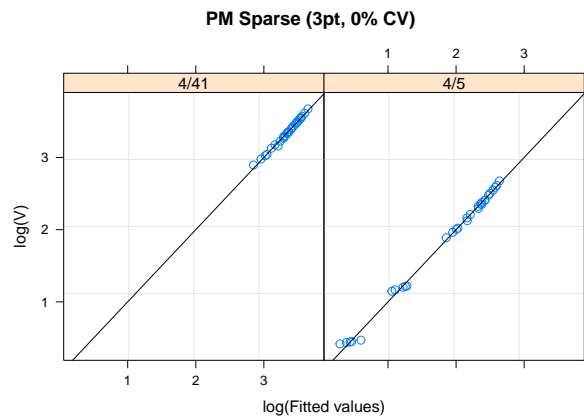
Sparse Study Designs (3pt)

```
par(mfrow = c(1, 2))
plot(PM_3pt_covar.nlm, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), xlab = "log(Fitted values)",
     main = "PM Sparse (3pt, 0% CV)")

plot(PM_3pt_CV5_covar.nlm, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), xlab = "log(Fitted values)",
     main = "PM Sparse (3pt, 5% CV)")

plot(PM_3pt_CV10_covar.nlm, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), xlab = "log(Fitted values)",
     main = "PM Sparse (3pt 10% CV)")

plot(PM_3pt_CV20_covar.nlm, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), xlab = "log(Fitted values)",
     main = "PM Sparse (3pt, 20% CV)")
```



Sparse Study Designs (4pt)

```
par(mfrow = c(1, 2))
plot(PM_4pt_covar.nlme, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), xlab = "log(Fitted values)",
     main = "PM Sparse (4pt, 0% CV)")

plot(PM_4pt_CV5_covar.nlme, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), xlab = "log(Fitted values)",
     main = "PM Sparse (4pt, 5% CV)")

plot(PM_4pt_CV10_covar.nlme, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), xlab = "log(Fitted values)",
     main = "PM Sparse (4pt, 10% CV)")

plot(PM_4pt_CV20_covar.nlme, log(V)~log(fitted(.))|Diplotype,
     abline = c(0,1), xlab = "log(Fitted values)",
     main = "PM Sparse (4pt, 20% CV)")
```

