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##################################################
## Non-linear growth function of time (t)
mu = function( t, beta0, beta1, theta, a, b){
beta0+beta1*t+theta*plogis(t, a, b)
}

##################################################
## NLME Model Fitting, with example starting values
library(nlme)
T = . # number of time points
n = . # number of mouse tumors
y = . # n by T array of tumor volume measurements, log transformed
day = . # T vector of days, on which tumor sizes were measured
data = data.frame(y=c(t(y)), t=rep(day[1:T],n),
                    mouse.id=as.factor(rep(1:n,each=T)))
data = groupedData(y~t|mouse.id,data)

nlme(y ~ mu(t,beta0,beta1,theta, a, b),
            data = data,
            fixed = list(beta0+beta1~1,theta + a + b ~ 1),
            random = beta0+beta1+theta + a + b ~ 1|mouse.id,
            start = c(beta0=4,beta1=0.18, theta = -3.5, a = 21, b = 4))


##################################################
## Non-linear Least Squares Model Fitting, with example starting values
T = . # number of time points
y = . # 1 by T array of tumor volume measurements, log transformed
t = . # T vector of time points (days), on which tumor sizes were measured

nls(y ~ mu(t,beta0,beta1,theta, a, b),
        algorithm="port",
         data = data,
        lower=c(2,.05,-10,6,1),upper=c(5,.22,  0,30,5),
        start = c(beta0=3.8,beta1=0.18,theta=-2,a=18,b = 3))

##################################################
## Piece-wise Model Fitting
f.pw = function(y, t, T, cp.i1, cp.i2){
## inputs:
## T = . # number of time points
## y = . # 1 by T array of tumor volume measurements, log transformed
## t = . # T vector of time points (days), on which tumor sizes were measured
## cp.i1 = . #  index of change point 1
## cp.i2 = . #  index of change point 2, > cp.i1

if(cp.i2>cp.i1){
index1=1:cp.i1
index2=(cp.i1+1):cp.i2
index3=(cp.i2+1):T
beta1 = lm(y[index1]~t[index1])$coef
y. = y[index2] - beta1[1]-beta1[2]*t[index2]
trend = -plogis(t[index2],(t[cp.i1+1]+t[cp.i2])/2,(t[cp.i2+1]-t[cp.i1])/7.33)
theta = lm(y.~0+trend)$coef
beta2 = lm(y[index3]~t[index3])$coef
mu = c(beta1[1]+beta1[2]*t[index1],beta1[1]+beta1[2]*t[index2]+theta*trend,
        beta2[1]+beta2[2]*t[index3])
sse = t(y-mu)%*%(y-mu)
return(list(beta1=beta1,theta=theta,beta2=beta2,fitted.logvol=mu,sse=sse))
}else{
print("Error, change points are not in increasing order")
}}
```