Project

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model

Here is a model of the virus's interaction with Human Small Airway Epithelial Cells (HSAEC). Based upon a modified version of the base model Benedict et al. (2015) where we added a viral decay parameter to simulate it closer to reality based upon Handel's influenza model Handel, Longini, and Antia (2009) . Used here are the standard situation (no drugs) parameters and values, displayed in this table.

Table 1: standard parameters and values

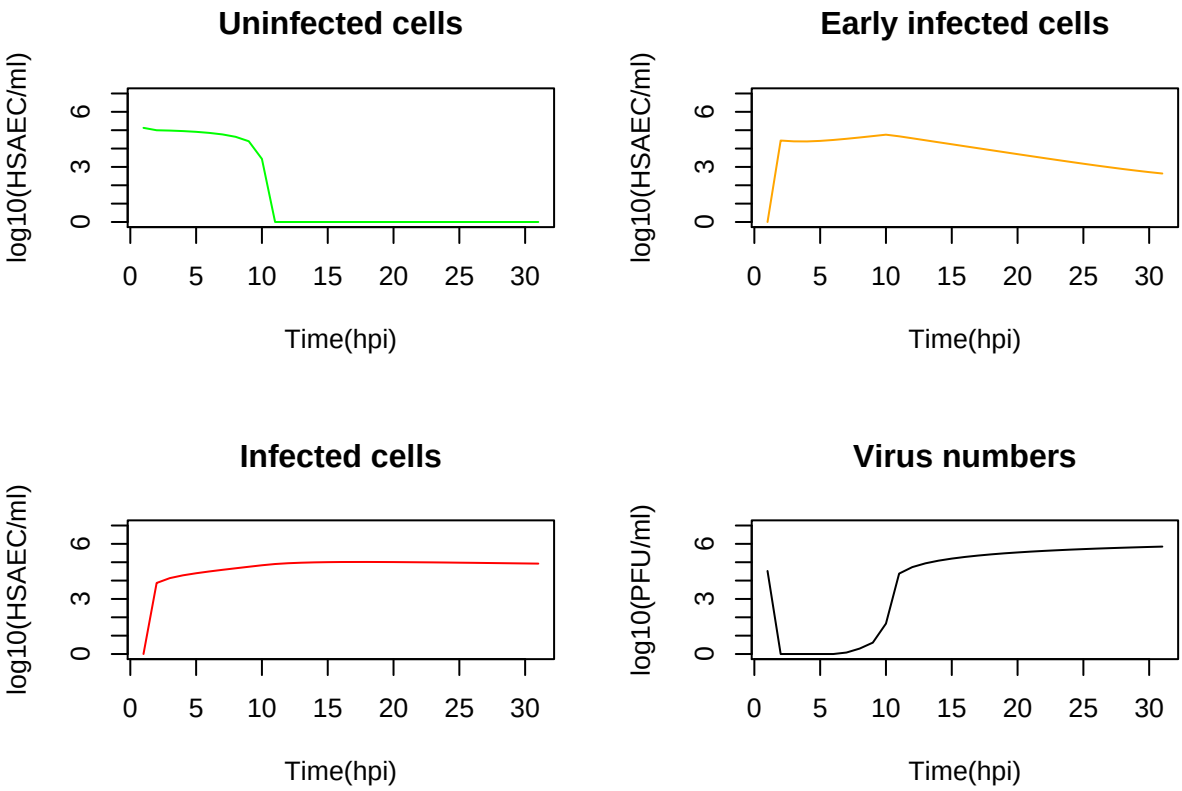
Symbol	Value
g	$0.742 * 10^{-3}$ h^{-1}
b	0.195 h^{-1} U^{-1}
l	1/4 h^{-1}
d	0.0222 h^{-1}
p	0.531 h^{-1}
vd	1/10 h^{-1}
U(0)	$1.34 * 10^5$ HSAEC/ml
E(0)	$3.34 * 10^4$ HSAEC/ml
I(0)	0 HSAEC/ml
V(0)	0 PFU/ml

```
# Parameters
parameters <- c(g = 0.742 * 10^-3, # h^-1
                b = 0.195, # h^-1 U^-1
                l = 1/4, # h^-1
                d = 0.0222, # h^-1
                p = 0.513 * 0.7, # h^-1
                vd = 0, # h^-1
                v = 1.00 # %
                )

# Initial state
y <- c(    U = 1.34 * 10^5, # HSAEC/ml
           E = 0, # HSAEC/ml
           I = 0, # HSAEC/ml
           V = 3.34 * 10^4, # PFU/ml
           D = 0
           )
# Model
viral <- function(t, y, parms){
  with(as.list(c(parms)),{
```

```
    dU <- g * y[5] - b * y[1] * y[4]
    dE <- b * y[1] * y[4] - l * y[2]
    dI <- l * y[2] - d * y[3]
    dV <- p * y[3] - b * y[1] * y[4] - vd *y[4]
    dD <- d * y[3] + (1-v) * y[1]  - g * y[5]
    return(list(c(dU, dE, dI, dV, dD)))
  })}
# Timeframe
times <- seq(0, 30, by = 1)
# Run model
viralout <- lsoda(y = y, times = times, parms = parameters, func = viral)
# Clean up data
viralout <- data.frame(viralout)
row.names(viralout) <- viralout$time
viralout <- viralout[2:6]
vir <- viralout
viralout <- apply(viralout, 2, log10)
viralout[is.na(viralout) | is.infinite(viralout) | viralout < 0] <- 0

#plot
par(mfrow=c(2,2))
#1
plot(viralout[,1], main = "Uninfected cells",
     xlab = "Time(hpi)", ylab = "log10(HSAEC/ml)",
     ylim = c(0, 7), type = "l", col = "green")
#2
plot(viralout[,2], main = "Early infected cells",
     xlab = "Time(hpi)", ylab = "log10(HSAEC/ml)",
     ylim = c(0, 7), type = "l", col = "orange")
#3
plot(viralout[,3], main = "Infected cells",
     xlab = "Time(hpi)", ylab = "log10(HSAEC/ml)",
     ylim = c(0, 7), type = "l", col = "red")
#4
plot(viralout[,4], main = "Virus numbers",
     xlab = "Time(hpi)", ylab = "log10(PFU/ml)",
     ylim = c(0, 7), type = "l")
```




```
par(mfrow=c(1,1))
#5
plot(viralout[,5], main = "Dead Cells",
     xlab = "Time(hpi)", ylab = "log10(HSAE/ml)",
     ylim = c(0, 7), type = "l")
```

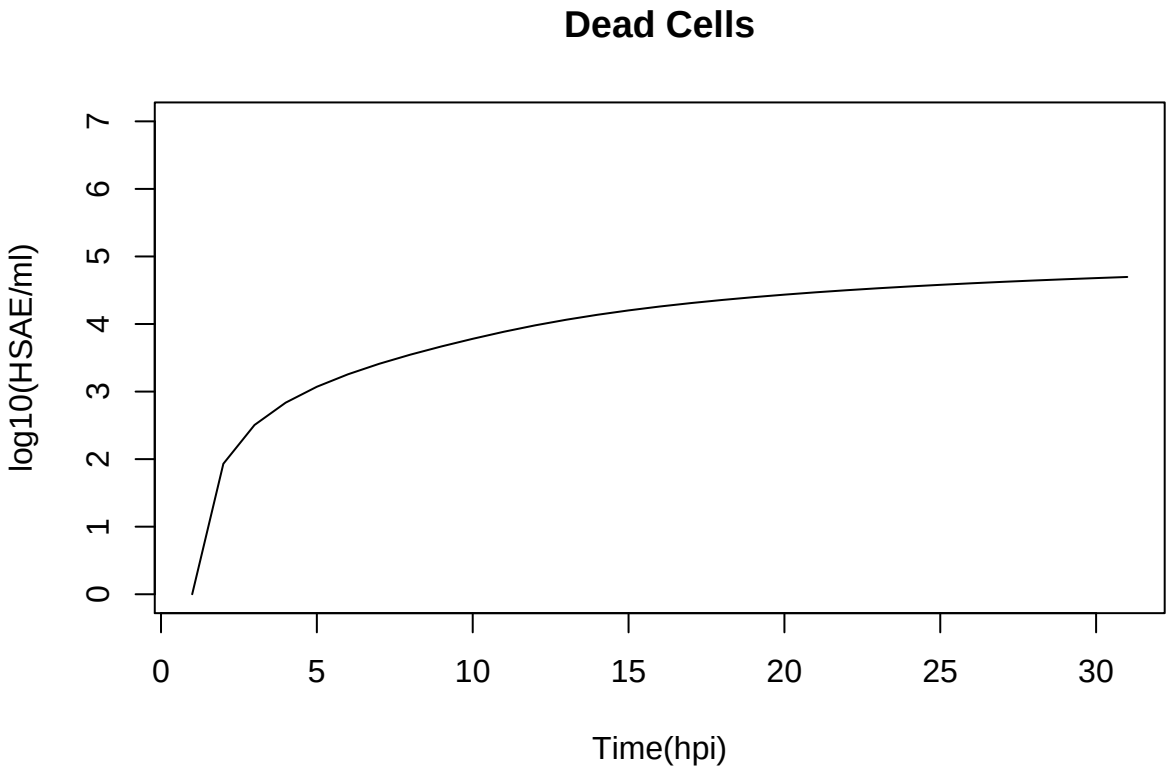


figure 6A from Benedict et al. (2015) shows bars with values

$1.05*10^6$ PFU/ml 108px
$1.40*10^5$ PFU/ml 93px
$3.10*10^3$ PFU/ml 63px

using log10(V values)/bar length is almost equal to 0.055

therefore to determine V when sorafenib was applied to the cell culture we will use the formula: $log10(V) = 0.055 * BarLength$.

```
V8 <- 0.055*43
V16 <- 0.055*46
V24 <- 0.055*41
```

Table 2: calculated values for treated cells

Time	BarLength	$log10(V)$	V
8	43	2.365	231.739465
16	46	2.53	338.8441561
24	41	2.255	179.8870915

Benedict, Ashwini, Neha Bansal, Svetlana Senina, Idris Hooper, Lindsay Lundberg, Cynthia de la Fuente, Aarthi Narayanan, Bradford Gutting, and Kylene Kehn-Hall. 2015. "Repurposing FDA-Approved Drugs as Therapeutics to Treat Rift Valley Fever Virus Infection." *Frontiers in Microbiology* 6 (July). https://doi.org/10.3389/fmicb.2015.00676.

Handel, Andreas, Ira M. Longini, and Rustom Antia. 2009. "Towards a Quantitative Understanding of the Within-Host Dynamics of Influenza A Infections." *Journal of The Royal Society Interface* 7 (42): 35–47. https://doi.org/10.1098/rsif.2009.0067.