

Appendix 1: R script for plantation malaria transmission model

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1 ### CAMBODIAN PLANTATION MALARIA TRANSMISSION MODEL: R CODE (10 AUGUST
... 2016) ###
2
3 #CLEAR WORKSPACE
4 rm(list=ls())
5
6 #LOAD LIBRARIES
7 library(deSolve)
8 library(ggplot2)
9
10 #MODEL DURATION (in years)
11 duration <- 10 # years
12 time.seq <- seq(0, duration*12, by = 1/30.415) # in months, by 1 day
... intervals
13
14 #MODEL PARAMETERS
15
16 #basic model parameters
17 nu=(1/(68.2*12)) # birth rate (1/life expectancy)
18 mu=(1/(68.2*12)) # death rate (1/life expectancy)
19 gamma=1/(11/30.415) # rate of movement from liver to asexual blood
... stage
20 delta=1/(10/30.415) # rate of gametocyte maturation
21 p=(0.93) # proportion of patients who are
... clinical/symptomatic(no immunity)
22 q=(0.50) # proportion of patients who are
... clinical/symptomatic(immunity)
23 tau=0.4 *** Proportion of clinical (symptomatic) patients
... treated.
24 zeta=1/(120/30.415) # rate of natural recovery from malaria infection
25 omega=1/(365/30.415) # rate of loss of immunity
26
27 # variable parameters (force of infection)
28 lagm=14/30.415 # time from mosquito biting infectious person until
... mosquito infectious
29 theta_cov=0.45 # coverage of vector control
30 theta_eff=0 # efficacy of vector control assuming 100% coverage
31 alpha=0.797 *** average number of bites per day
32 amp=0.9 # relative amplitude of seasonal forcing
33 phi=8 # month of peak in seasonal forcing
34
35 # Migration parameters
36 magi=1 # Amplitude of migration
37 eta=0.37 # proportion of workers on plantations who are
... migrant workers
38 phi2=5 # month of peak in migrant worker immigration
39 phi3=12 # month of peak in migrant worker emigration
40 ksi=0.00 # prevalence of malaria in area from which
... migrants come
41
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42 #PCR Paramaters
43 PCR_interv_start= 12*3 # duration in months until MDA
... intervention begins
44 PCR_interv_end= (12*3) + 1/30.415 # duration in months PCR campaign
45 PCR_cov= 0 # coverage of PCR campaign
46 PCR_eff= 1.0*0.9 # reduction in transmission given
... full PCR coverage
47
48 # population parameters
49 worker_pop <- 10000
50 initN <- worker_pop*(1-eta) # initial population of plantation(s)
51 M <- worker_pop*(eta) # migrant workers per year
52 prev <- 0.0284 # prevalence of asymptomatic chronic
... infections
53 # on plantation(s)
54
55 # MODEL INITIAL CONDITIONS: S -> L1 -> A1 -> G1 -> R ( -> S) -> L2 -> A2
... -> G2 (-> R)
56 initR <- 0 # initial treated compartment (partial immunity)
57 initL1 <- 0 # initial liver1 stage compartment (no immunity)
58 initA1 <- 0 # initial asexual1 blood-stage compartment (no
... immunity)
59 initG1 <- 0 # initial sexual1 gametocyte blood-stage
... compartment (no immunity)
60 initL2 <- 0 # initial liver2 stage compartment (with partial
... immunity)
61 initA2 <- 0 # initial asexual2 blood-stage compartmen ( partial
... immunity)
62 initG2 <- prev*initN # initial gametocyte2 blood-stage compartment (
... partial immunity)
63
64 # initial susceptible compartment
65 initS <- initN-initL1-initA1-initG1-initR-initL2-initA2-initG2
66
67 state <- c(S = initS, L1 = initL1, A1 = initA1, G1 = initG1,
68 R = initR, L2=initL2, A2 = initA2, G2 = initG2)
69
70 #MODEL FUNCTION
71 malaria<-function(t, state, parameters)
72 {
73
74 # Parameters
75
76 parameters <- c(
77 # basic model parameters
78 nu=nu, # birth rate (1/life expectancy)
79 mu=mu, # death rate (1/life expectancy)
80 gamma=gamma, # rate of movement from liver to asexual blood stage
81 delta=delta, # rate of gametocyte maturation
82 p=p, # proportion of patients who are clinical/symptomatic

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82... (no immunity)
83     q=q,          # proportion of patients who are clinical/symptomatic
... (immunity)
84     tau=tau,      # Proportion of clinical (symptomatic) patients
... treated
85     zeta=zeta,    # rate of natural recovery from malaria infection
86     omega=omega,  # rate of loss of immunity = 1/(average duration of
... immunity)
87
88     # variable parameters (force of infection)
89     lagm=lagm,    # time from mosquito biting infectious person, until
... mosquito infectious
90     alpha=alpha,  # average number of bites per day
91     theta_cov=theta_cov, # coverage of vector control
92     theta_eff=theta_eff, # efficacy of vector control assuming 100%
... coverage
93     amp=amp,      # relative amplitude of seasonal forcing
94     phi=phi,      # week of peak in seasonal forcing
95
96     #PCR Paramaters
97     PCR_interv_start=PCR_interv_start,    # Start PCR intervention
98     PCR_interv_end=PCR_interv_end,        # duration in weeks of PCR
... drug effect
99     PCR_cov=PCR_cov,                      # coverage of PCR campaign
100    PCR_eff=PCR_eff,                      # reduction in
... transmission:full PCR coverage
101
102    # Migration parameters
103    magi=magi,          # speed of migration
104    eta=eta,            # proportion of workers on plantations who are
... migrant workers
105    phi2=phi2,          # month of peak in migrant worker immigration
106    phi3=phi3,          # month of peak in migrant worker emigration
107    ksi=ksi
108 )
109
110 with(as.list(c(state, parameters)),
111     {
112
113     # Define lag in Gt (G total) -- the number of people in
... compartments G1 and G2
114     # at the time mosquitoes were infected "lagm" weeks prior
115     #(ie. time it takes from mosquito bite until the mosquito is
... infectious)
116
117     if (t<=lagm)
118         Gt <- initG1 + initG2
119
120     else
121         Gt <- lagvalue(t=t-lagm,nr=4) + lagvalue(t=t-lagm,nr=8)

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122
123     # variables
124     N     <- (S+L1+A1+G1+R+L2+A2+G2)
125     seas <- 1+amp*cos(2*pi*(t-phi)/12)
126     beta <- (1-theta_cov*theta_eff)*alpha*(Gt/N)
127     lam  <- beta*seas
128
129     # Migration variables
130     iota <- 0 #magi*(1+cos(2*pi*(t-phi2)/12))/12 # rate of
... immigration
131     eps <- 0 #magi*(1+cos(2*pi*(t-phi3)/12))/12 # rate of
... emigration
132     ion<-ceiling(t %% 12)== phi2
133     eon<-ceiling(t %% 12)== phi3
134
135     #PCR Campaign
136     PCR <-
... (PCR_cov*PCR_eff)*(t>(PCR_interv_start))*(t<=(PCR_interv_start+
... PCR_interv_end))
137
138     # rate of change
139     dS <- nu*N-mu*S-lam*S+omega*R-eps*M*S/N+
140         iota*M*(1-ksi)-eon*(S/N)*M+(1-ksi)*ion*M
141     dL1 <- -mu*L1+lam*S-gamma*L1-eps*M*L1/N-eon*(L1/N)*M
142     dA1 <-
... -mu*A1+gamma*L1-(delta/(1-p*tau))*A1-eps*M*A1/N-eon*(A1/N)*M-PCR*A1
143     dG1 <-
... -mu*G1+delta*A1-(zeta/(1-p*tau))*G1-eps*M*G1/N-eon*(G1/N)*M-PCR*G1
144     dR <-
... ((delta*p*tau)/(1-p*tau))*A1+(zeta/(1-p*tau))*G1+((delta*q*tau)/
145     (1-q*tau))*A2+(zeta/(1-q*tau))*G2-(mu+lam+omega)*R-eps*M*R/N-eon*(R/N)*M+
146     PCR*(A1+G1)+PCR*(A2+G2)
147     dL2 <- -mu*L2+lam*R-gamma*L2-eps*M*L2/N-eon*(L2/N)*M
148     dA2 <-
... -mu*A2+gamma*L2-(delta/(1-q*tau))*A2-eps*M*A2/N-eon*(A2/N)*M-PCR*A2
149     dG2 <- -mu*G2+delta*A2-(zeta/(1-q*tau))*G2-eps*M*G2/N+
150     iota*M*(ksi)-eon*(G2/N)*M+ksi*ion*M-PCR*G2
151
152     # return the rate of change
153     list(c(dS, dL1, dA1, dG1, dR, dL2, dA2, dG2))
154   })}
155
156   #MODEL OUTPUT
157   out <- dede(y = state, times = time.seq, func = malaria, parms =
... parameters)
158   pop <- out[, "S"]+out[, "L1"]+out[, "A1"]+out[, "G1"]+out[, "R"]+out[, "L2"]+
159     out[, "A2"]+out[, "G2"]
160   time <- out[, "time"]
161   OUT <- data.frame(out)

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162 OUT$Gt <- OUT$G1 + OUT$G2
163 OUT$N <- OUT$S + OUT$L1 + OUT$A1 + OUT$G1 + OUT$R + OUT$L2 + OUT$A2 +
... OUT$G2
164 # Percentage population prevalence (asymptomatic and symptomatic people
... in blood stage)
165 OUT$Prevalence.perc <- ((OUT$A1 + OUT$G1 + OUT$A2 + OUT$G2)/OUT$N)*100
166 # Population prevalence (asymptomatic and symptomatic people in blood
... stage)
167 OUT$Prevalence.pop <- (OUT$A1 + OUT$G1 + OUT$A2 + OUT$G2)
168 # Monthly reported incidence = blood stages: symptomatic & received
... treatment)
169 OUT$Incidence <- ((delta*p*tau)/(1-p*tau))*OUT$A1 + zeta*OUT$G1 +
170 ((delta*q*tau)/(1-q*tau))*OUT$A2
171 #Proportion of cases with no immunity / partial immunity
172 OUT$Clinical <- (OUT$A1 + OUT$G1)/(OUT$A2 + OUT$G2)
173 OUT$year <- time/12
174
175 # function to round up to nearest hundred
176 roundUpNice <- function(x, nice=c(1,2,4,5,6,8,10)) {
177 if(length(x) != 1) stop("'x' must be of length 1")
178 10^floor(log10(x)) * nice[which(x <= 10^floor(log10(x)) * nice)[[1]]]
179 }
180
181 #####
182
183 #MODEL PLOTS
184
185 #Change format of dataframe so that all compartments/states are in one
... column,
186 #count in 2nd column, year in 3rd column
187 cbPalette <- c("light blue", "dark blue", "red", "maroon", "green", "dark
... green",
188 "black", "yellow")
189 Stab<-cbind(cbind(rep('S',length(time.seq)),as.numeric(OUT$S)),OUT$year)
190
... L1tab<-cbind(cbind(rep('L1',length(time.seq)),as.numeric(OUT$L1)),OUT$year)
191
... A1tab<-cbind(cbind(rep('A1',length(time.seq)),as.numeric(OUT$A1)),OUT$year)
192
... G1tab<-cbind(cbind(rep('G1',length(time.seq)),as.numeric(OUT$G1)),OUT$year)
193 Rtab<-cbind(cbind(rep('R',length(time.seq)),as.numeric(OUT$R)),OUT$year)
194
... L2tab<-cbind(cbind(rep('L2',length(time.seq)),as.numeric(OUT$L2)),OUT$year)
195
... A2tab<-cbind(cbind(rep('A2',length(time.seq)),as.numeric(OUT$A2)),OUT$year)
196
... G2tab<-cbind(cbind(rep('G2',length(time.seq)),as.numeric(OUT$G2)),OUT$year)
197 Prev.perc.tab<-cbind(cbind(rep('Prevalence',length(time.seq)),
198 as.numeric(OUT$Prevalence.perc)),OUT$year)
199 Prev.pop.tab<-cbind(cbind(rep('Prevalence',length(time.seq)),

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200   as.numeric(OUT$Prevalence.pop)),OUT$year)
201   Inctab<-cbind(cbind(rep('Incidence',length(time.seq)),
202   as.numeric(OUT$Incidence)),OUT$year)
203   MMWInctab<-cbind(cbind(rep('Incidence',length(time.seq)),
204   as.numeric(OUT$Incidence)),OUT$year)
205   MMWInctab[,2] <- as.integer(MMWInctab[,2]) # proportion of people treated
... by the MMW
206   MMWInctab[,2] <- (as.integer(MMWInctab[,2])/initN)*1000 # incidence per
... 1000 population
207
208   # Plot 1: All compartments
209   dd<-as.data.frame(rbind(Stab,L1tab,A1tab,G1tab,Rtab,L2tab,A2tab,G2tab))
210   colnames(dd)<-c('State','Count','Year')
211   dd$Count<-as.numeric(as.character(dd$Count))
212   dd$Year<-as.numeric(as.character(dd$Year))
213
214   p1 <- ggplot(data=dd,aes(x=Year,y=Count,group=State,color=State)) +
215     geom_line(size=1) +
216     theme_bw()+
217
... scale_colour_manual(values=cbPalette,breaks=c("S","L1","A1","G1","R","L2","
... A2","G2"))+
218     labs(title = "Compartmental model of malaria transmission", x="Year",
219           y="Plantation inhabitants") +
220     theme(legend.title=element_blank()) +
221     theme(plot.title = element_text(lineheight=.8, face="bold")) +
222     theme(legend.key = element_blank())
223     p1
224
225   # Plot 2: All compartments, except susceptible population
226   dd2<-as.data.frame(rbind(L1tab,A1tab,G1tab,Rtab,L2tab,A2tab,G2tab))
227   colnames(dd2)<-c('State','Count','Year')
228   dd2$Count<-as.numeric(as.character(dd2$Count))
229   dd2$Year<-as.numeric(as.character(dd2$Year))
230
231   p2 <- ggplot(data=dd2,aes(x=Year,y=Count,group=State,color=State)) +
232     geom_line(size=1) +
233     theme_bw()+
234
... scale_colour_manual(values=cbPalette,breaks=c("L1","A1","G1","R","L2","A2",
... "G2")) +
235     labs(title = "Compartmental model of malaria transmission",
236           x="Year", y="Plantation inhabitants") +
237     theme(legend.title=element_blank()) +
238     theme(plot.title = element_text(lineheight=.8, face="bold")) +
239     theme(legend.key = element_blank())
240     p2
241
242   # Plot 3: Infected compartments
243   dd3<-as.data.frame(rbind(L1tab,A1tab,G1tab,L2tab,A2tab,G2tab))

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```

244 colnames(dd3)<-c('State','Count','Year')
245 dd3$Count<-as.numeric(as.character(dd3$Count))
246 dd3$Year<-as.numeric(as.character(dd3$Year))
247
248 p3 <- ggplot(data=dd3,aes(x=Year,y=Count,group=State,color=State)) +
249   geom_line(size=1) +
250   theme_bw()+
251
252   ... scale_colour_manual(values=cbPalette,breaks=c("L1","A1","G1","R","L2","A2",
253   "G2")) +
254   labs(title = "Compartmental model of malaria transmission",
255         x="Year", y="Plantation inhabitants") +
256   theme(legend.title=element_blank()) +
257   theme(plot.title = element_text(lineheight=.8, face="bold")) +
258   theme(legend.key = element_blank())
259   p3
260
261 # Plot 4: Prevalence
262 dd4<-as.data.frame(rbind(Prev.perc.tab))
263 colnames(dd4)<-c('State','Count','Year')
264 dd4$Count<-as.numeric(as.character(dd4$Count))
265 dd4$Year<-as.numeric(as.character(dd4$Year))
266
267 p4 <- ggplot(data=dd4,aes(x=Year,y=Count, color="red")) +
268   geom_line(size=1) +
269   theme_bw()+
270   theme(plot.title = element_text(lineheight=.8, face="bold")) +
271   labs(title = "Malaria prevalence on plantations", x="Year",
272   ... y="Prevalence (%)") +
273   theme(legend.position="none")
274   p4
275
276 dd4$Date <- seq.Date(as.Date("01/01/07", "%d/%m/%y"), by = "day",
277   ... length.out = 3650)
278 plot(dd4[2373:3102,4],dd4[2373:3102,2],type = 'l',
279   main="Model vs data for plantation prevalence\nin Mondulkiri Province"
280   ... ,
281   col="black",lwd=2, ylim=c(0,5), xlab="Month", ylab = "Prevalence %")
282 points(dd4[2709,4],0,col= "red", pch = 19) #MK 0-2.84, ST 0.53-1.68
283 arrows(dd4[2709,4],0,dd4[2709,4],0.67,length=0.05, angle=90,
284   ... code=3,col="red")
285 points(dd4[2831,4],2.84,col= "red", pch = 19)
286 arrows(dd4[2831,4],1.59,dd4[2831,4],5,length=0.05, angle=90,
287   ... code=3,col="red")
288 legend("bottomleft", inset=.05,
289   c("Model  ", "Data  "), fill=c("black","red"), horiz=TRUE)
290
291 dd4$Date <- seq.Date(as.Date("01/01/07", "%d/%m/%y"), by = "day",
292   ... length.out = 3650)
293 plot(dd4[2373:3102,4],dd4[2373:3102,2],type = 'l',

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286     main="Model vs data for plantation prevalence\nin Stung Treng
... Province",
287     col="black",lwd=3, ylim=c(0,3.7), xlab="Month", ylab ="Prevalence %")
288     points(dd4[2709,4],0.53,col= "red", pch = 19) #MK 0-2.84, ST 0.53-1.68
289     arrows(dd4[2709,4],0.18,dd4[2709,4],1.56,length=0.05, angle=90,
... code=3,col="red")
290     points(dd4[2831,4],1.68,col= "red", pch = 19)
291     arrows(dd4[2831,4],0.77,dd4[2831,4],3.61,length=0.05, angle=90,
... code=3,col="red")
292     legend("bottomleft", inset=.05,
293           c("Model  ", "Data  "), fill=c("black","red"), horiz=TRUE)
294
295     # Plot 5: Incidence
296     MMWInctab <- as.data.frame(rbind(MMWInctab))
297     colnames(MMWInctab)<-c('State','Count','Year')
298     MMWInctab$Count<-as.numeric(as.character(MMWInctab$Count))
299     MMWInctab$Year<-as.numeric(as.character(MMWInctab$Year))
300
301     p5 <- ggplot(data=MMWInctab,aes(x=Year,y=Count,color="red")) +
302       geom_line(size=1) +
303       theme_bw()+
304       labs(title = "Malaria incidence on plantations", x="Year",
305            y="Treated symptomatic cases \nper 1000 plantation inhabitants") +
306       theme(legend.title=element_blank()) +
307       theme(plot.title = element_text(lineheight=.8, face="bold")) +
308       theme(legend.position="none")
309     p5
310
311     MMWInctab$Date <- seq.Date(as.Date("01/01/07","%d/%m/%y"),
312                               by = "day", length.out = 3650)
313     plot(MMWInctab[1095:3650,4],MMWInctab[1095:3650,2]*1/4,type = 'l',
314          col="black",lwd=2, ylab = "Incidence per 1000 population", xlab="")
315
316     # Plot 6: Phase plot
317     plot(MMWInctab[,2],Prev.perc.tab[,2], type = 'l',
318          xlab = "Incidence of symptomatic cases per 1000 plantation
... inhabitants",
319          ylab = "Prevalence (%)", main = "Phase plot of incidence vs
... prevalence",
320          col="red", lwd =2)
321
322     # Plot 7: Total population N
323     plot(time,OUT$N,type="l",ylim=c(0,11000), ylab = "N")

```