Les matemàtiques i la dinàmica de les malalties infeccioses

Universitat de València

David Alonso

Grup de recerca en ecologia teòrica i computational

CEAB-CSIC

http://theelab.net/ dalonso@ceab.csic.es

May 25, 2020

"L'acte pedagògic no és una simple juxtaposició d'intervencions individuals, per molt afinades que siguin, sinó una construcció, tant material com simbòlica, de l'escola en el seu principi mateix: aprendre junts gràcies a la figura tutelar del professor que, a el mateix temps, crea alguna cosa comú i acompanya cadascun en la seva singularitat. *Aquesta dialèctica entre el col·lectiu i l'individu, el descobriment del que uneix els alumnes i el que especifica a cada un d'ells, és, de fet, el que «fa una escola»*"

Texte paru dans
LE CAFE PEDAGOGIQUE
du 17 avril 2020 de Philippe Meirieu

MACARTHUR ON ECOLOGY

Stephen D. Fretwell
Division of Biology, Kansas State University, Manhattan, Kansas 66506

Every word of God is tested.

Proverbs 30:5

PROLOGUE

Scientists are responsible for truth, knowledge, wisdom, and understanding.

Truth is what is—it is the underlying reality of all existence. Knowledge is what we think we know about truth. Knowledge, however, is always an imperfect assessment, and is always subject to revision and improvement. The realization that there are discrepancies and weaknesses in knowledge is wisdom. Wisdom leads to a process, called the philosophy of science, through which knowledge is modified to better fit the truth. Philosophy means the love of wisdom, and doctors of philosophy are supposed, before all else, to be experts in wisdom. Understanding, as defined in Job (28:28), is the effort to avoid evil. We may think of understanding as what we use in order to adequately apply our wisdom and our knowledge in guiding our actions. While applied scientists seek understanding, basic scientists seek knowledge.

Dr. Robert MacArthur has made a dramatic impact on ecology because, to him, all of this was second nature.

Qué pretende la investigación científica?

"... First, to permit an adequate *description* of the things and events that are the objects of scientific investigation; second, to permit the establishment of general laws or theories by means of which particular events may be *explained* and *predicted*"

C.G. Hempel (1965: 139, emphasis original),
Aspects of Scientific Explanation

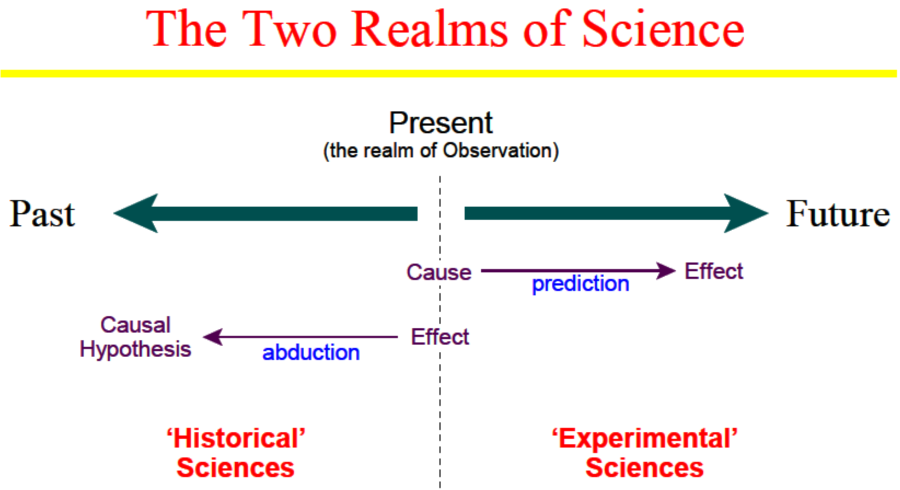
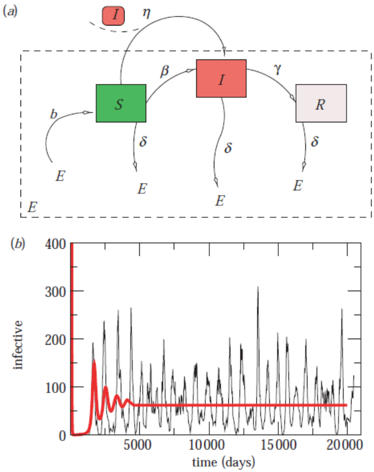


Figura adaptada del curso
"The Philosophy of Biological Systematics"
Kirk Fitzhugh
Natural History Museum, Los Angeles, USA.



$$\frac{dS}{dt} = -\beta \frac{I}{N} S$$
$$\frac{dI}{dt} = \beta \frac{I}{N} S - \gamma I$$
$$\frac{dR}{dt} = \gamma I$$

The force of infection: $\lambda = \hat{\beta}\, b\, \frac{I}{N}$

A l'inici: $S \approx N$,

$$\frac{dI}{dt} = \hat{\beta}\, b \frac{I}{N} S - \gamma I$$

$$\frac{dI}{dt} = \left(\hat{\beta}\, b - \gamma\right) I$$

Alonso, McKane & Pascual 2007. Interface

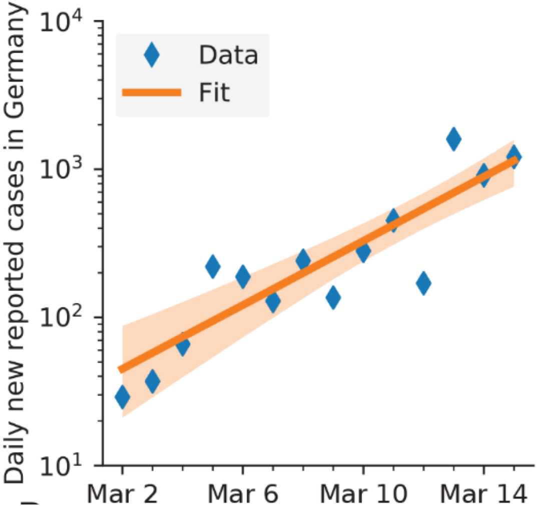
Stochastic amplification in epidemics

$$I(t) = I_0 \; e^{\left(\hat{\beta}\, b - \gamma\right)\, t}$$

$$\log(I(t)) = \log(I_0) + m\, t$$

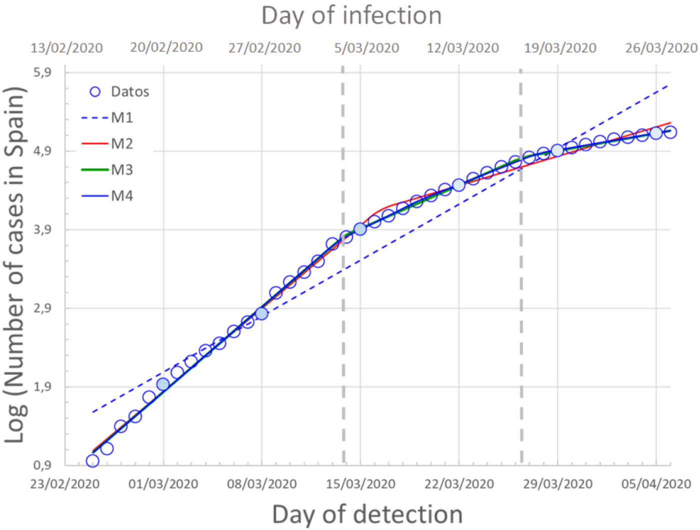
$$m = \left(\hat{\beta}\, b\, - \gamma\right)$$

$$R_0 = \frac{\hat{\beta}\, b}{\gamma}$$



J. Dehning et al., 2020

Science `10.1126/science.abb9789`



Santamaría & Hotal, 2020

`https://www.medrxiv.org/content/10.1101/2020.04.09.20059345v3.full`

R_0

- Número d'infeccions que cada infectat és capaç de crear mentre està infectat en una població completament susceptible (a l'inici de l'epidèmia)

$$R_0 = \text{(Taxa d'encontre)} \; \text{(Infectivitat)} \; \text{(Temps Durada Infecció)}$$

- Número d'infeccions que cada infectat és capaç de crear mentre està infectat (al llarg de l'epidèmia)

$$R_{eff} = \text{(Taxa d'encontre)} \, \frac{S}{N} \; \text{(Infectivitat)} \; \text{(Temps Durada Infecció)}$$

- "How do mathematicians model infectious disease outbreaks?" by Robin Thomson
  `https://livestream.com/oxuni/thompson`
- 3blue1brown on youtube
  `https://youtu.be/gxAaO2rsdIs`
  `https://www.3blue1brown.com`
- "Modeling infectious disease dynamics:
  The spread of the coronavirus SARS-CoV-2 has predictable features"
  by Sarah Cobey
  `http://science.sciencemag.org/` on May 16, 2020
- NetLogo
  `https://ccl.northwestern.edu/netlogo/`
- Mosquito alert
  `http://www.mosquitoalert.com/ca/`

Índice

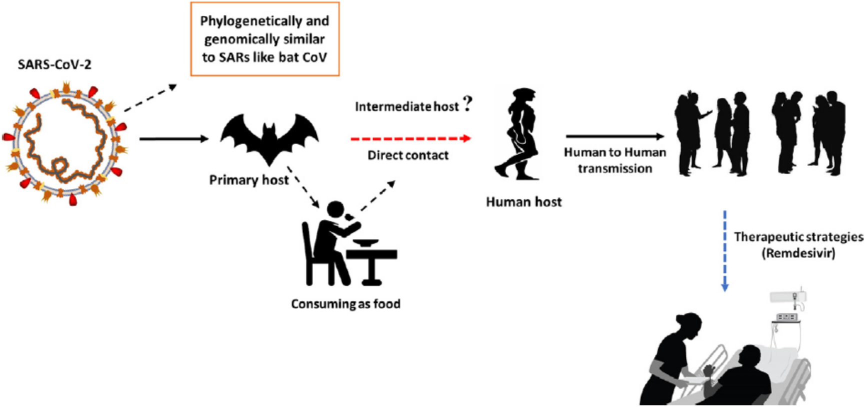


Figura de M.A. Shereen et al. Journal of Advanced Research 24 (2020) 91–98

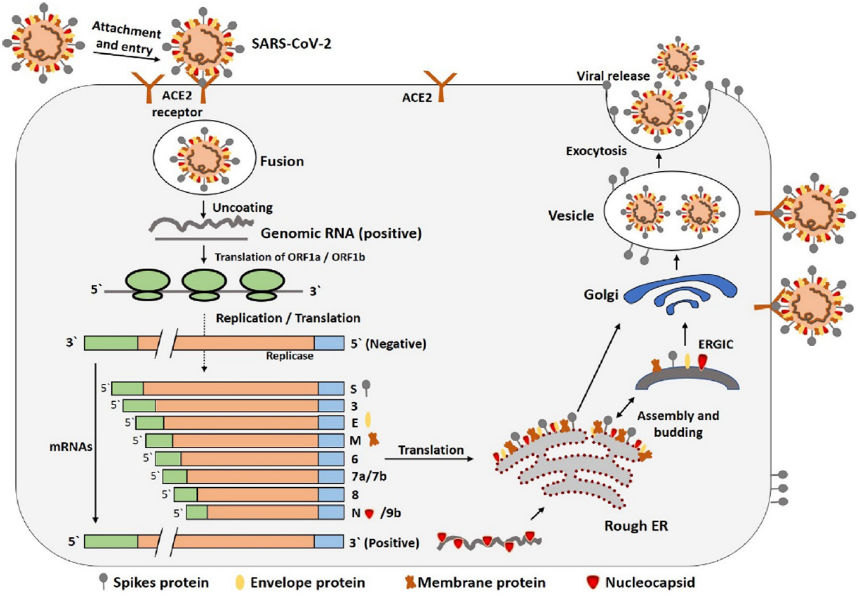
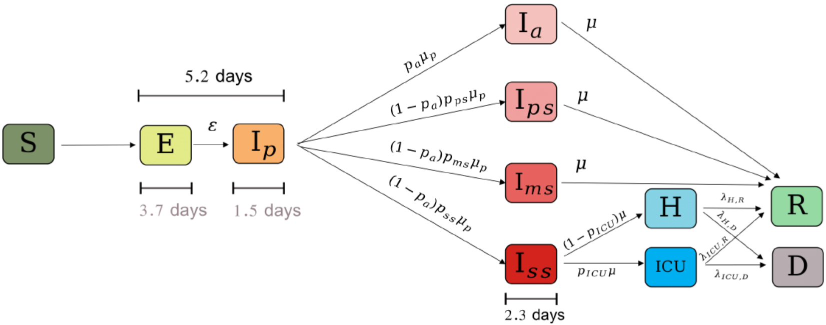
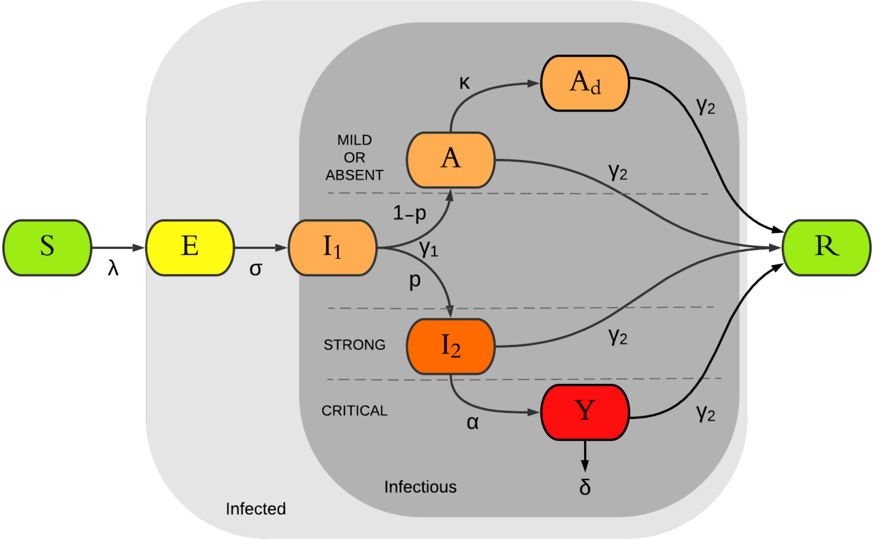


Figura de M.A. Shereen et al. Journal of Advanced Research 24 (2020) 91–98

Model Francès



Expected impact of lockdown in Île-de-France and possible exit strategies
Laura Di Domenico *etal*
medRxiv preprint doi: https://doi.org/10.1101/2020.04.13.20063933



A metapopulation model for covid19 transmission
David Alonso and Frederic Bartumeus
En preparación

Model Parameter	Symbol
Demographic and movement-related parameters	
Population size of the *i*-th age class at the *j*-t city	P_{ij}
Movement rate from city *k* into city *j*	μ_{jk}
Disease transmission parameters	
Contact rate between age group *k* and *i*	β_{ik}
Detectability rate of assymtomatics	κ
Average infectivity	b
Pre-symptomatic infectivity factor	ϕ
Isolation effectiveness of strong cases	ϵ_I
Isolation effectiveness of serious cases	ϵ_Y
Rate of appearance of infectious ability	σ
Rate of appearance of symptoms	γ_1
Age-dependent probability for strong symptoms	p_i
Age-dependent rate of appearence of serious symptoms	α_i
Age-dependent disease-induced mortality	δ_i
Rate of recovery	γ_2

Impacto de las medidas de distanciamiento social sobre la expansión de la epidemia de COVID-19 en España (CSIC)

Objetivos:

- Integración de datos masivos a tiempo real de movilidad humana y encuestas geolocalizadas en modelos de transmisión de covid19.
- La investigación propuesta permitirá comprender mejor los efectos de las medidas de restricción de movilidad y distanciamiento social sobre la dinámica epidemiológica que rige la propagación de la enfermedad.
- El proyecto se respalda en herramientas matemáticas y computacionales, desarrolladas por los distintos miembros del equipo de trabajo, algunas ya en marcha.

PI: José Javier Ramasco (IFISC) & Frederic Bartumeus (CEAB)

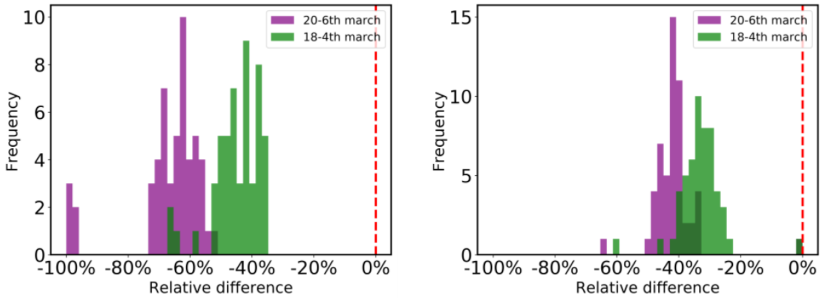


Figura 8: Diferencia relativa de la movilidad interprovincial (izquierda) y la movilidad intraprovincial (derecha) para todas las provincias del viernes 6 al 20 (violeta) y del miércoles 4 al 18 (verde).

http://analytics.ifisc.uib-csic.es/es/respuesta-covid-19/

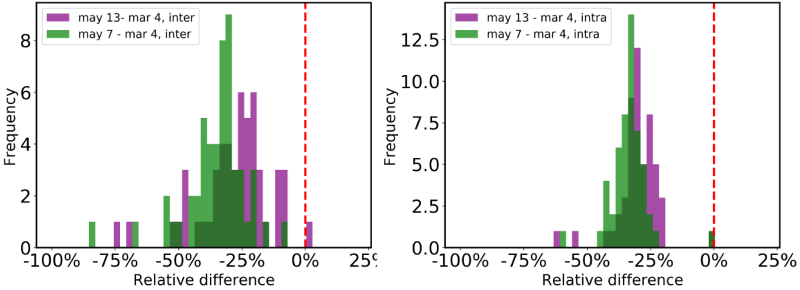
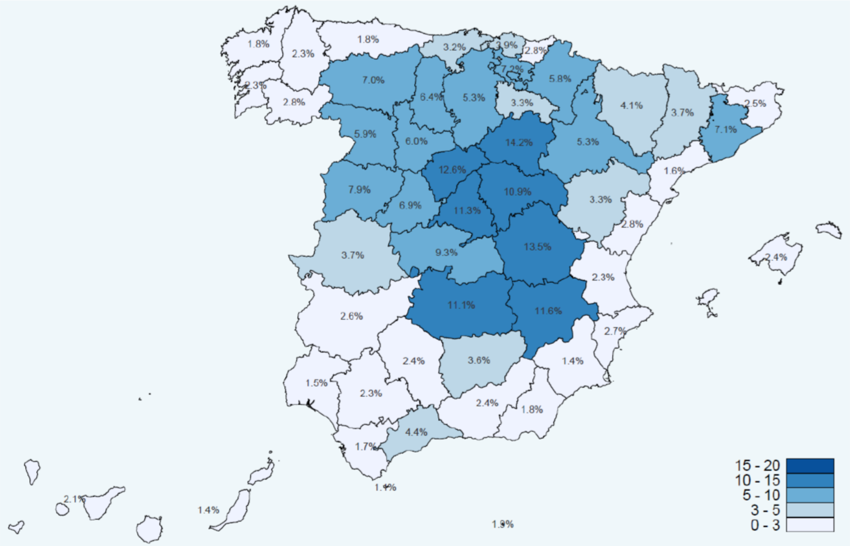


Figure 1: Diferencia relativa de movilidad externa (izquierda) y movilidad interna (derecha) para todas las provincias de España entre los miércoles 4 de marzo y 7 y 13 de mayo.

http://analytics.ifisc.uib-csic.es/es/respuesta-covid-19/

Mapa provincial de Anticuerpos IgG anti SARS-Cov2



Aedes aegypti biting *Homo sapiens*
(source: upload.wikimedia.org)

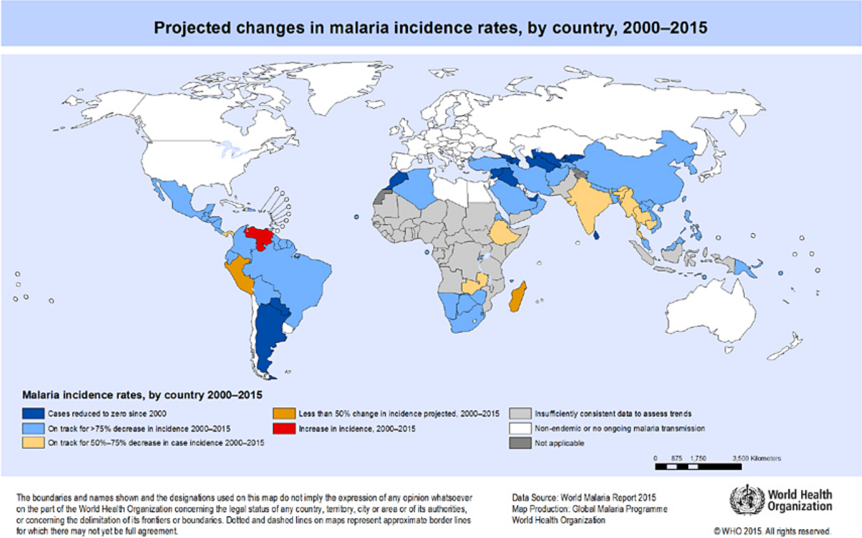
- Environmental change
- Socio-economic factors
- Emergence of infectious diseases

Aedes aegypti biting *Homo sapiens*
(source: upload.wikimedia.org)

Anopheles mosquitoes

Anopheles albimanus
(source: `www.answers.com`)

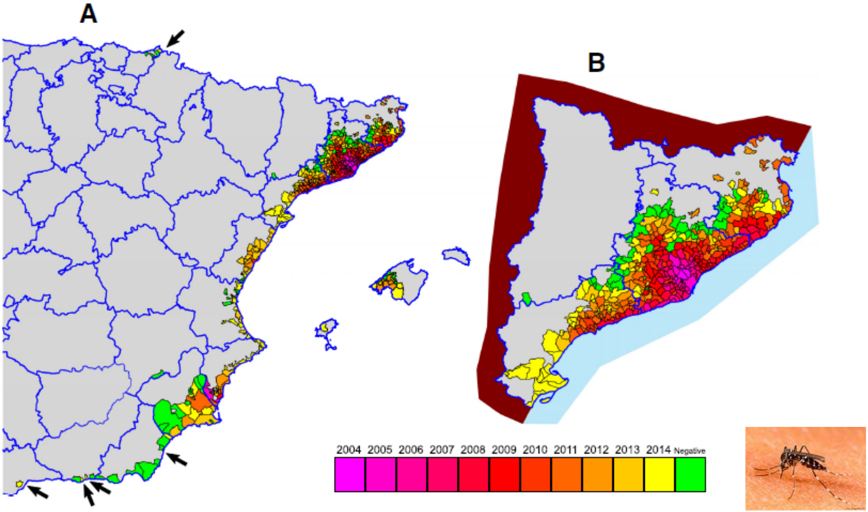
Anopheles gambiae
(source: `entomology.ucdavis.edu`)



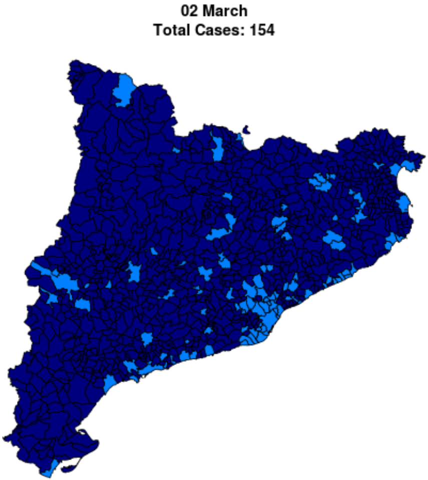
Cases	Deaths	Funding
216 million	445 000	2.7 billion $ (2016)


MOSQUITO ALERT
Projecte
Info mosquits
Àmbits d'actuació
Sobre nosaltres
Blog
Ciència ciutadana per investigar i controlar mosquits transmissors de malalties
Unim la ciutadania, científics i gestors de salut pública i medi ambient per lluitar contra el mosquit tigre i el mosquit de la febre groga, vectors de Zika, Dengue i Chikungunya
Descarrega l'app i avisa si veus mosquits tigre o de la febre groga
Disponible a App Store
DISPONIBLE A Google Play
Consulta el mapa per veure les troballes de tot el món a temps real
Accedeix al mapa

The Invasion of Tiger Mosquito in Spain (2004-2014)



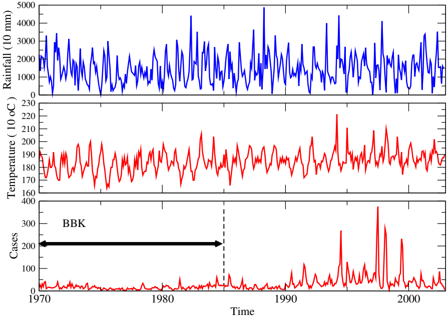
Chikungunya: Prevention and Control



Data from simulation

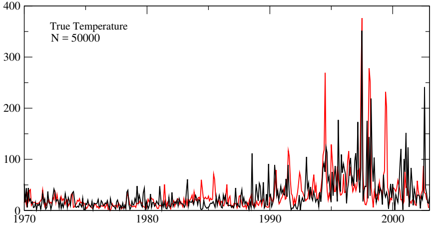
- Imported Chikungunya cases since 2008
- Autochthonous transmision in Italy and France
- Chikungunya Outbreak of Denge in 2013 in Portugal

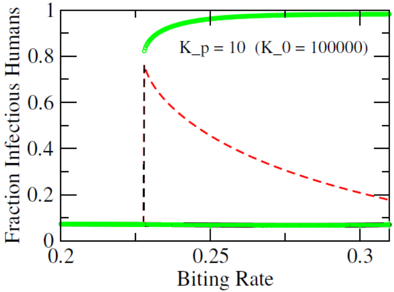
Palmer *etal* (in prep)



PREDICTED (best solution) vs EMPIRICAL MONTHLY CASES

Fitting the whole time series (black) vs empirical data (red)





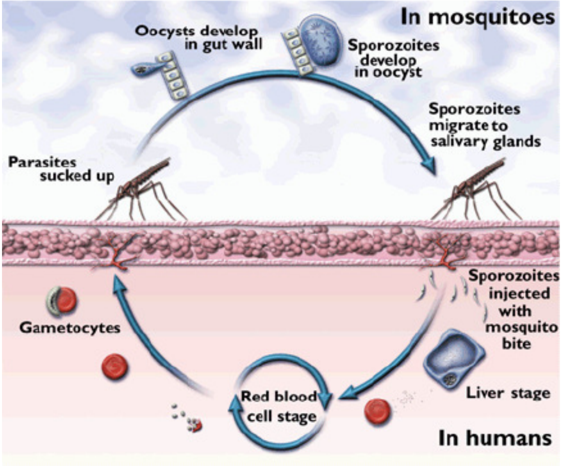
Alonso, D., Bouma, M. J., & Pascual, M. (2011)

Proceedings. Biological Sciences. The Royal Society

Alonso, D., Dobson, A, & Pascual, M. (2019)

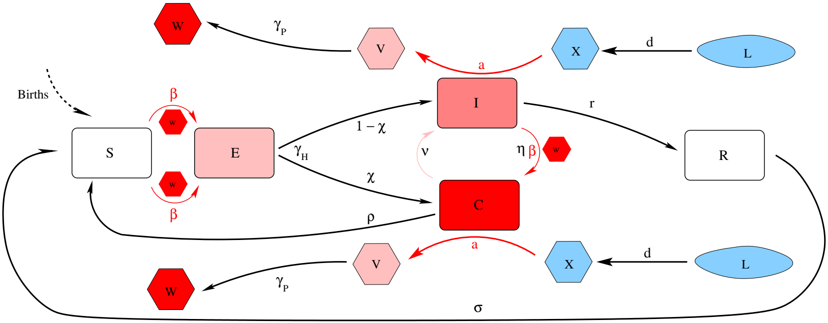
Phil. Trans. R. Soc. B 374

Human - Mosquito - *Plasmodium*



(source: `www.cbu.edu`)

Human-Mosquito coupled model



Alonso, D., Dobson, A, & Pascual, M. (2019)

Phil. Trans. of The Royal Society

Human model

β, the force of infection

$$
\begin{aligned}
\frac{dS}{dt} &= B - \beta\, S + \sigma R - \delta\, S + \rho\, C \\
\frac{dE}{dt} &= \beta\, S - \delta\, E - \gamma\, E \\
\frac{dI}{dt} &= (1 - \xi)\,\gamma\, E - \eta\,\beta\, I + \nu\, C - r\, I - \delta\, I \\
\frac{dR}{dt} &= -\sigma R + r\, I - \delta\, R \\
\frac{dC}{dt} &= \xi\,\gamma\, E + \eta\,\beta\, I - \nu\, C - \rho\, C - \delta\, C
\end{aligned}
$$

Human model

β, the force of infection

$$
\begin{aligned}
\frac{dS}{dt} &= B - \beta\, S + \sigma R - \delta\, S + \rho\, C \\
\frac{dE}{dt} &= \beta\, S - \delta\, E - \gamma\, E \\
\frac{dI}{dt} &= (1-\xi)\,\gamma\, E - \eta\,\beta\, I + \nu\, C - \mathbf{r}\, I - \delta\, I \\
\frac{dR}{dt} &= -\sigma R + \mathbf{r}\, I - \delta\, R \\
\frac{dC}{dt} &= \xi\,\gamma\, E + \eta\,\beta\, I - \nu\, C - \rho\, C - \delta\, C
\end{aligned}
$$

Human immunity

- The rate of loss of immunity, σ, and the recovery rate, r are related to the intensity of disease transmission.
- If the frequency of infectious bites increases both the recovery rate, r, and the loss of immunity rate, σ, tend to decrease.
- The rate at which infectious bites per human arrive is

$$\Lambda = a\frac{W}{N}$$

:

$$\sigma(\Lambda) = \frac{\Lambda}{\exp(\Lambda/\sigma_0) - 1}$$

$$r(\Lambda) = \frac{\Lambda}{\exp(\Lambda/r_0) - 1}$$

Dietz 1979; Aron and May 1982

Human model: parameters

6	Human turnover	δ
7	Incuvation rate	γ
8	Immunity loss rate	σ_0
9	Recovery from I	r_0
10	Recovery from C	ρ
11	Recovery from C to I	ν
12	Probability $I \longrightarrow C$	η
13	Probability $S \longrightarrow C$	ξ

The force of infection:

$$\beta = b\, a\, \frac{W}{N} + \beta_0$$

Mosquito model: Population dynamics

L, larval stage and M adult stage

$$\frac{dL}{dt} = f\,M\left(\frac{K-L}{K}\right) - \delta_L\,L - d_L\,L$$
$$\frac{dM}{dt} = d_L\,L - \delta\,M$$

Mosquito carrying capacity is controlled by water availability.

$$\frac{dK}{dt} = K_A\,p - K_E\,K$$

Mosquito model: parameters

1	Fecundity	f
2	Carrying capacity	K
3	Larval development	d_L
4	Larval mortality	δ_L
5	Adult mortality	δ_M

Mosquito carrying capacity is controlled by water availability...

$$\frac{dK}{dt} = K_A \, p - K_E \, K$$

Mosquito model: Infectious dynamics

$$
\begin{aligned}
\frac{dL}{dt} &= f\,M\left(\frac{K-L}{K}\right) - \delta_L\,L - d_L\,L \\
\frac{dX}{dt} &= -c\,a\,y\,X - \delta_M\,X + d_L\,L \\
\frac{dV}{dt} &= +c\,a\,y\,X - \gamma_P\,V - \delta_M\,V \\
\frac{dW}{dt} &= \gamma_P\,V - \delta_M\,W
\end{aligned}
$$

where y is the fraction of infectious humans:

$$
y = \frac{C+I}{H}
$$

Mosquito model: Population dynamics

$$\frac{dL}{dt} = f\, M \left(\frac{K - L}{K}\right) - \delta_L\, L - d_L\, L$$
$$\frac{dM}{dt} = d_L\, L - \delta_M\, M$$

where y is the fraction of infectious humans:

$$y = \frac{C + I}{N}$$

14	*Plasmodium* Incubation rate	γ_P

Mosquito model: Parameter Response Curves

The model incorporates 5 response curves for 5 different parameters (temperature-driven parameters):

- Development rate of the mosquito larvae, d_L:

$$d_L = 0.00554\, T - 0.06737$$

- Development rate of the *Plasmodium* parasite, γ_P
- Death rate of adult mosquitoes, δ_M
- Death rate of mosquitoes larvae, δ_L
- Gonotrophic cycle and mosquito fecundity, a and F

Mosquito model: temperature-driven parameters

- Larva development, d_L
- *Plasmodium development,* γ_P
- Adult and larval survival, δ_M, δ_L
- Biting rate, a

$$f = F\,a$$

where F is the number of eggs per female.

Effective temperature experimented by adult mosquitoes:

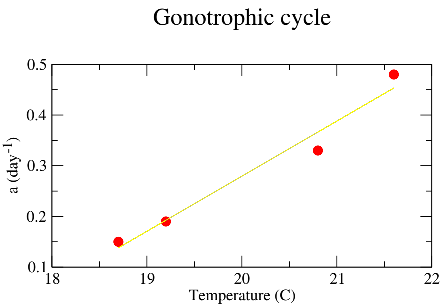
$$T_e = T_o + (1 - x)\,\Delta T$$

Mosquito model: temperature-driven parameters

- Larva development, d_L
- *Plasmodium development,* γ_P
- Adult and larval survival, δ_M, δ_L
- Biting rate, a

$$f = F\,a$$

where F is the number of eggs per female.



Afrane, Y. A., B. W. Lawson, A. K. Githeko and G. Yan (2005) *J. Med. Entomology*

Effective temperature experimented by adult mosquitoes:

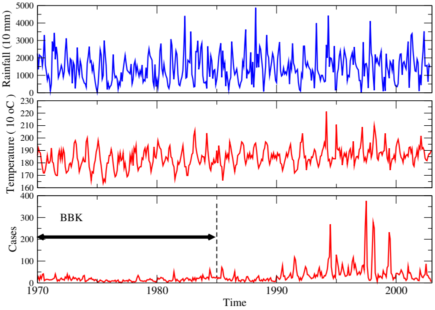
$$T_e = T_o + (1 - x)\,\Delta T$$

Temperature and Adult Mosquitoes

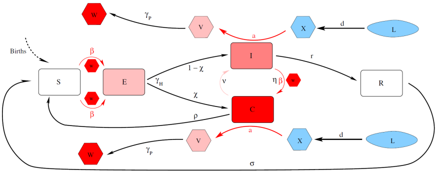
"...that if a mosquito is to become infective, it must spend all its time inside an occupied hut. It probably makes flights to a pool of water for oviposition, but rapidly return to the warm shelter of the hut"

"It is apparently only because *A. gambiae* and *A. funestus* are essentially hut insects that malaria occurs at all at places over 1500 m. or so"

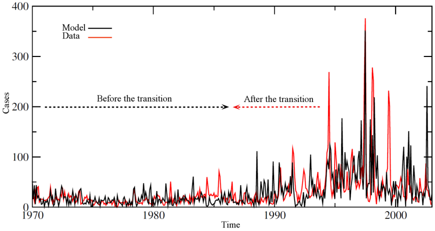
Garnham, P. (1948). The incidence of malaria at high altitudes. *J. Natl. Mal. Soc.*, 7, 453 275-284.



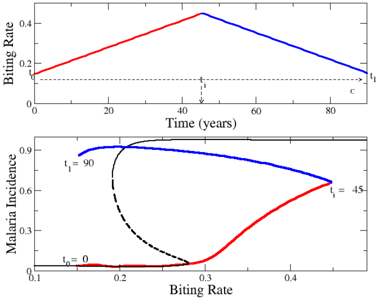
(a) Data



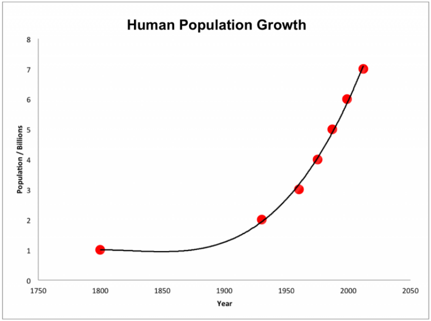
(b) Model



(c) Model Prediction

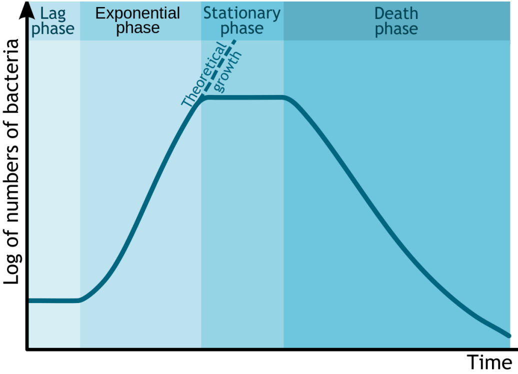


(d) Hysteresis



"It's been 20 years since the Day of 6 Billion"

Posted by Deborah Byrd in HUMAN WORLD October 12, 2019

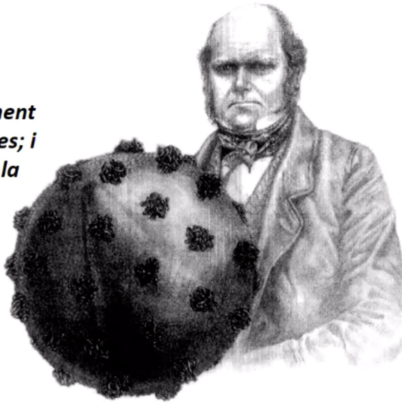


"Bacterial Growth"

https://en.wikipedia.org

"Quan una espècie augmenta desordenadament en un periode curt, sovint apareixen epidèmies; i aquí tenim un filtre limitant, independent de la lluita per la vida."

Charles Darwin
On the Origin of Species



de Xavier López-labrador "Nou coronavirus: qui t'avisa no et vol mal" a la Matinal de l'Evolució, UV, aquesta matinal

ciberesp · GENERALITAT VALENCIANA · Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana · CENTRE SUPERIOR INVESTIGACIÓ EN SALUT PÚBLICA · Global Influenza Hospital Surveillance Network

"The world is stranger than we can imagine and surprises are inevitable in science. Thus, we found, for example, that pesticides increases pests, antibiotics can create pathogens, agricultural development creates hunger, and flood control leads to flooding. But some of these surprises could have been avoided if the problems had been posed big enough to accomodate solutions in the context of the whole"

"Les sorpreses en ciència són inevitables. Així, per exemple, trobem que els pesticides incrementen las plagues, els antibiótics poden crear patógens més perillosos, la tecnificació de l'agricultura crea fam y el control de les inundacions condueix a inundacions majors. Tanmateix, la majoria d'aquestes sorpreses podríen evitar-se si analitzéssim els problemes en un context més ampli." (R. Levins)

T. Awerbuch, A. E. Kiszeweski, and R. Levins (2002). "Surprise, non-linearity, and complex behavior" (chap 4) a: Environmental Change, Climate and Health: Issues and Research Methods editat per P. Martens, A. J. McMichael. Cambridge University Press