Análise crítica de modelos matemáticos utilizados para modelar a dinâmica populacional de *Aedes aegypti*

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IBEX, 25 de agosto de 2011

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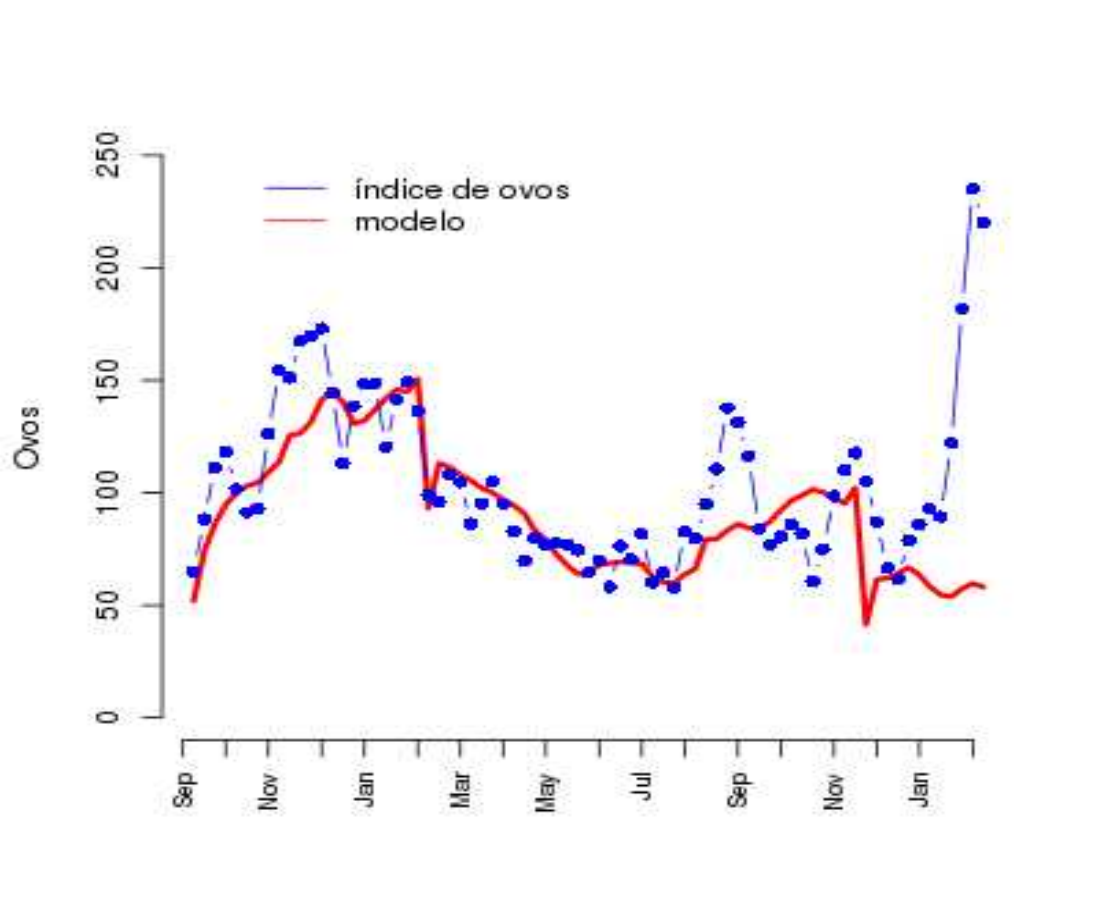
- Moacyr Silva e Flavio Coelho (FGV)
- Rede Pronex de Modelagem em Dengue (Fiocruz, FGV, IMPA, USP, UFF, Unioeste, UFMA, UFMG, UFOP, UFLA)

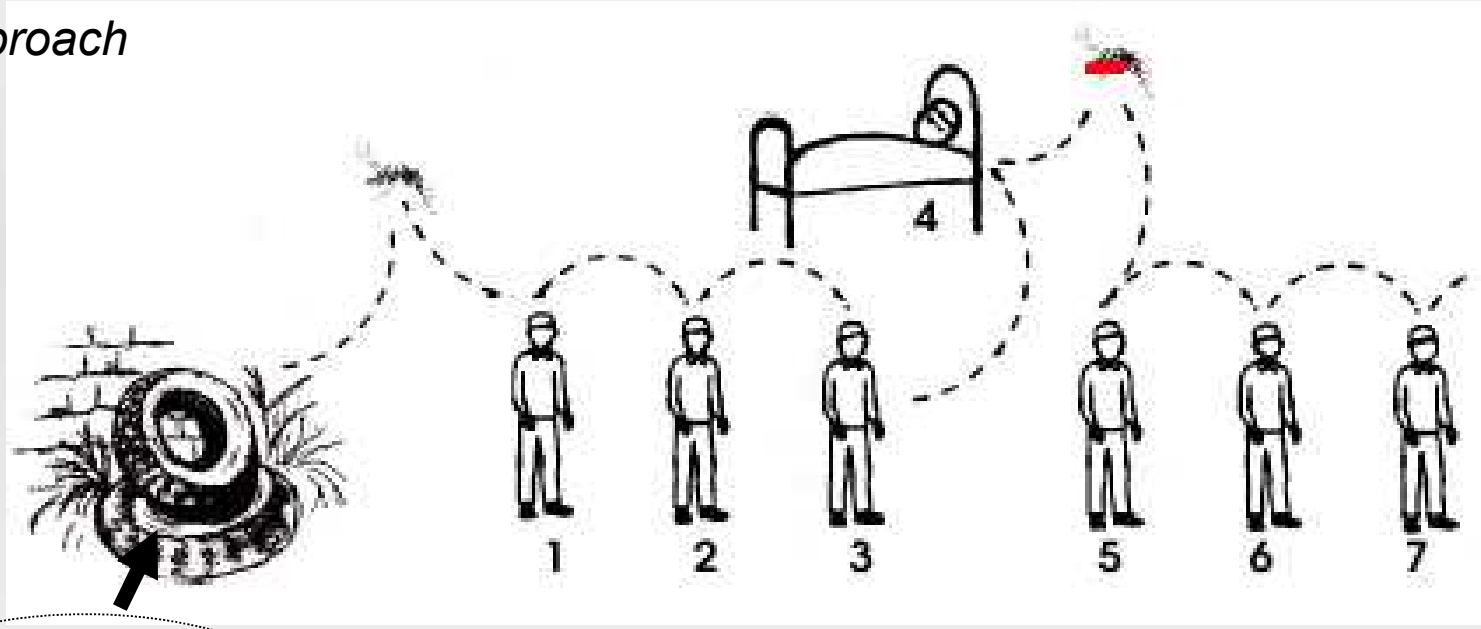
Modelo de dinâmica populacional

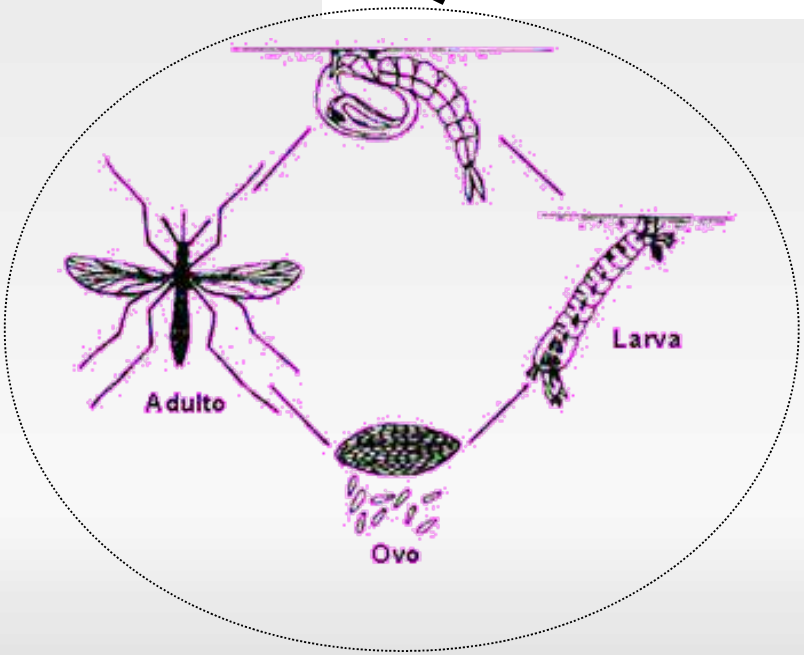


Dados de Honório et al (2009), Modelo de Lana et al (2011)

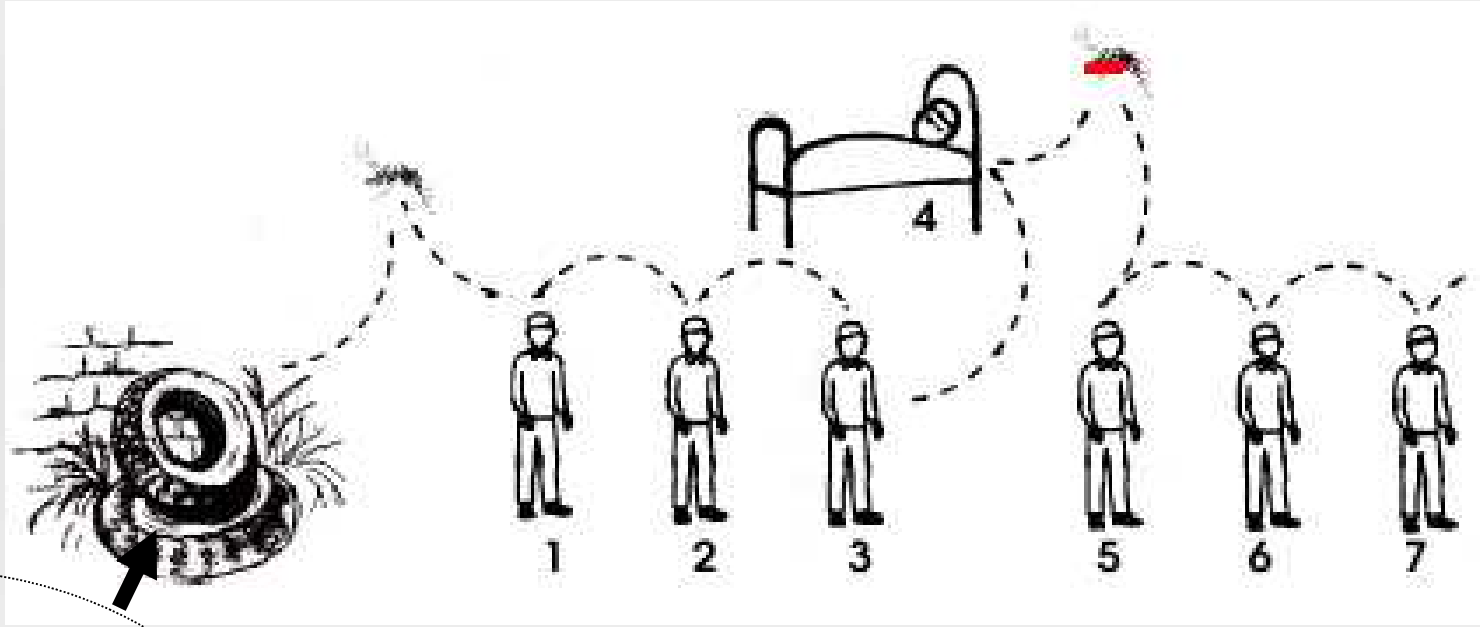
Modelo de dinâmica populacional

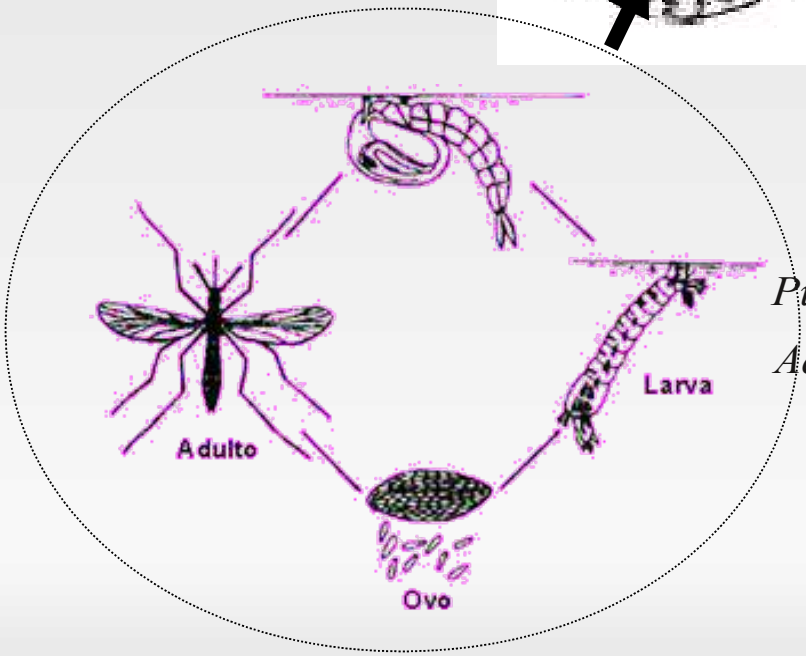
First principles approach





Modelo de dinâmica populacional





$$Ovos(t+1) = Ovos(t) - eclosão(\Delta t) + oviposição(\Delta t) - mortos(\Delta t)$$

$$Larvas(t+1) = Larvas(t) + eclosão(\Delta t) - pupação(\Delta t) - mortos(\Delta t)$$

$$Pupas(t+1) = Pupas(t)(\Delta t) + pupação(\Delta t) - emergência(\Delta t) - mortos(\Delta t$$

$$Adultos(t+1) = Adultos(t)(\Delta t) + emergência(\Delta t) - mortos(\Delta t)$$

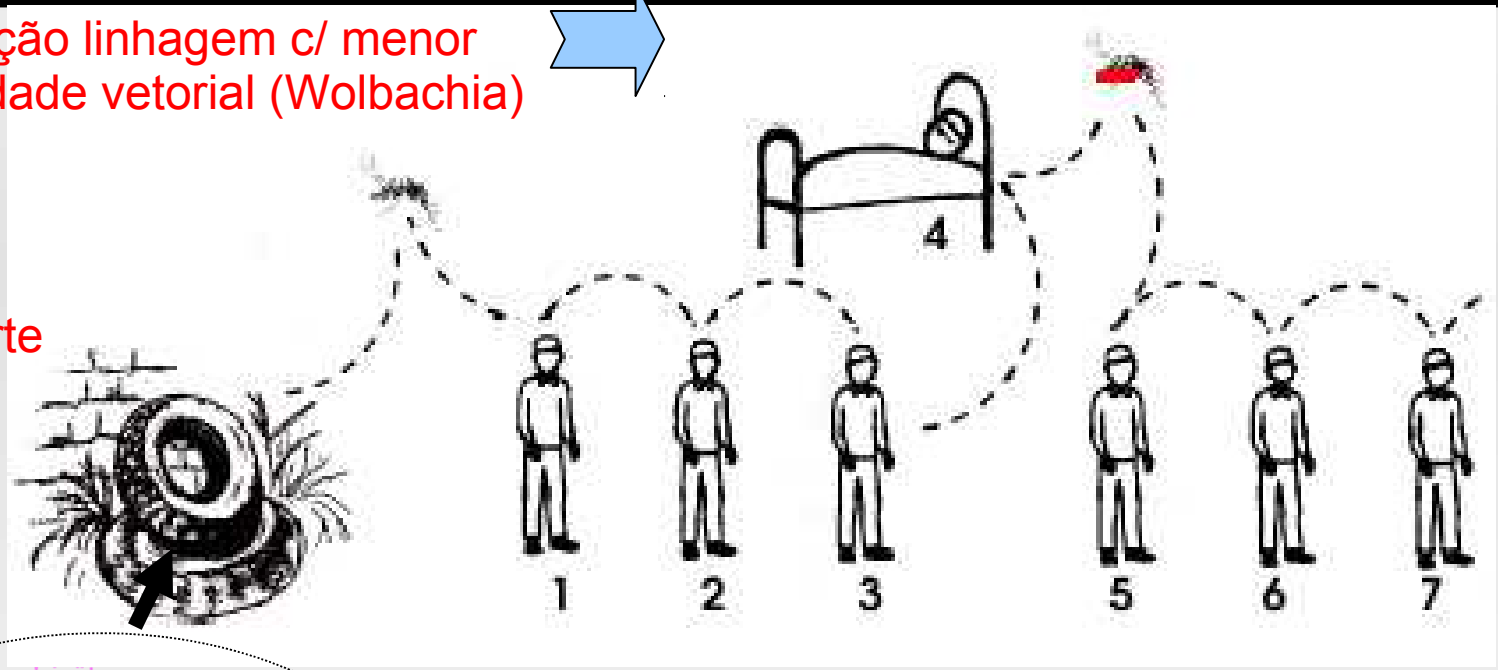
Dificuldades:

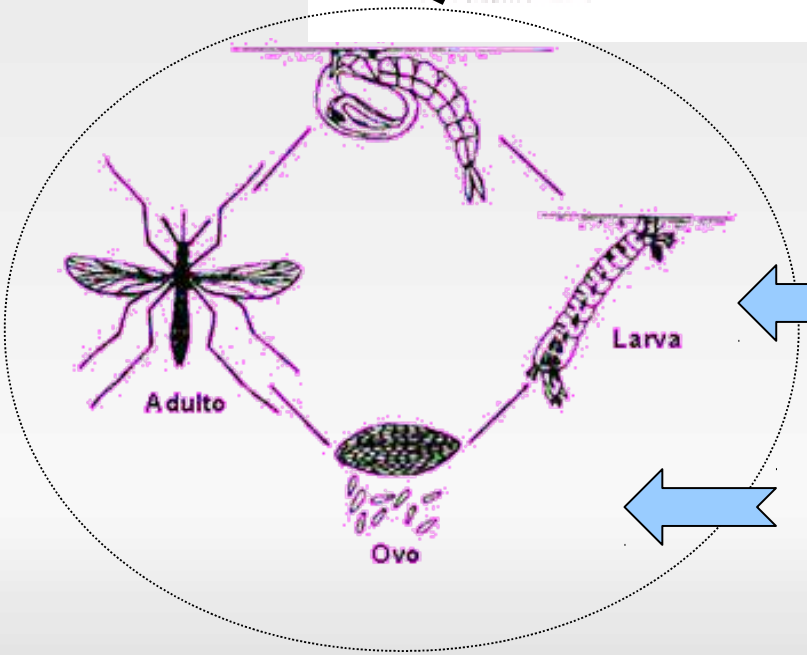
- Pocessos dependentes da densidade
- Processos dependentes do ambiente (clima)
- Interações entre os dois

Modelo como laboratório de ideias

Introdução linhagem c/ menor capacidade vetorial (Wolbachia)

Redução da Capacidade de suporte





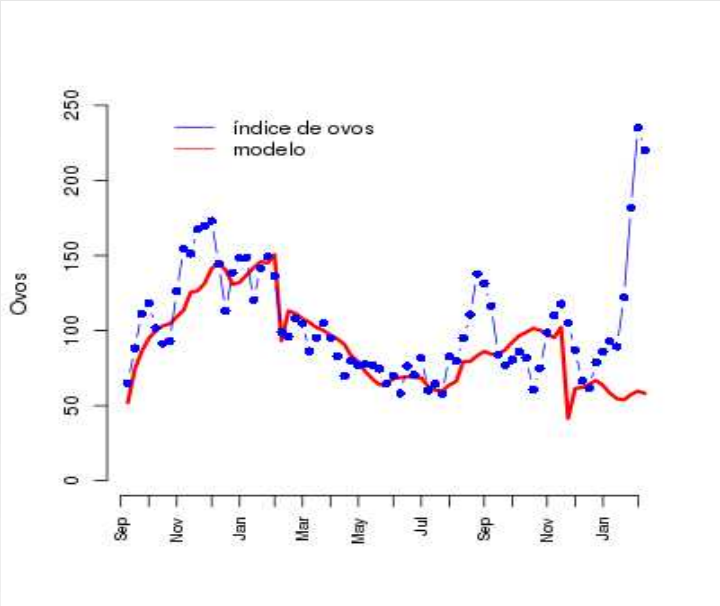
larvicidas

Remoção intensiva de ovos (inundação De armadilhas)

Introdução Machos estéreis

Validação de um modelo

(1) Confrontação com os dados populacionais



(2) Gerar predições testáveis

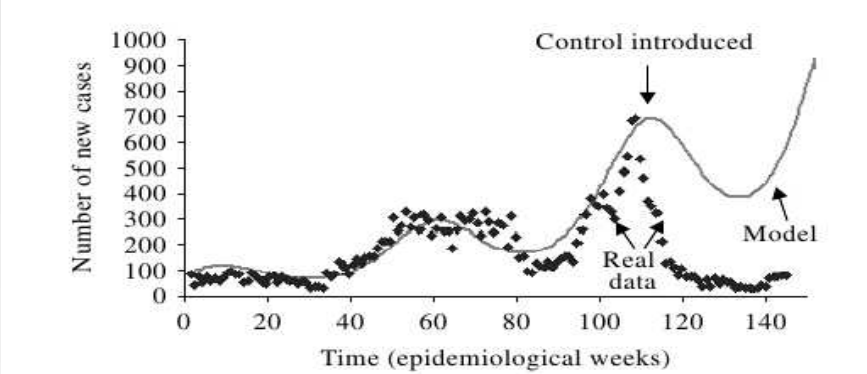


Fig. 4. Simulation of the projected number of cases if the control programme was not introduced in October 2005, compared with real data (from http://www.moh.gov.sg/cmaweb/attachments/publication).

Buratini et al, 2008

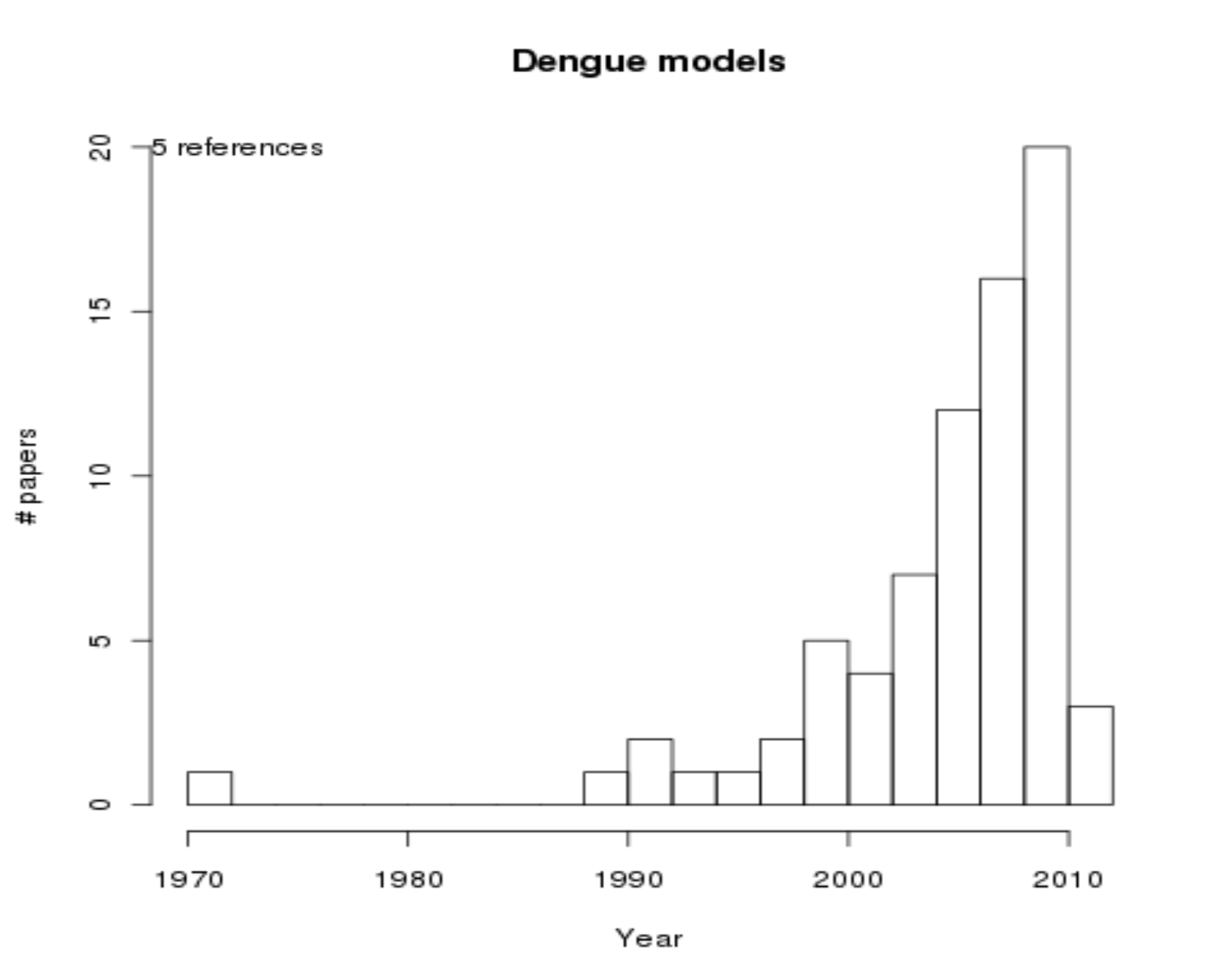
(3) Consistência, validade, confiança em seus pressupostos

Proposta de trabalho

- Rever modelo(s) de dinâmica populacional de Aedes aegypti na literatura
- Identificar a validade biológica de seus pressupostos
  - Opinião de especialistas
  - Literatura
- Identificar lacunas de conhecimento biológico e teórico

Dengue mathematical models in MedLine (n = 75)

N = 75



- exclui artigos de modelagem teóricos onde a dengue aparece como “desculpa”
- exclui artigos que modela Aedes aegypti desvinculado da dengue

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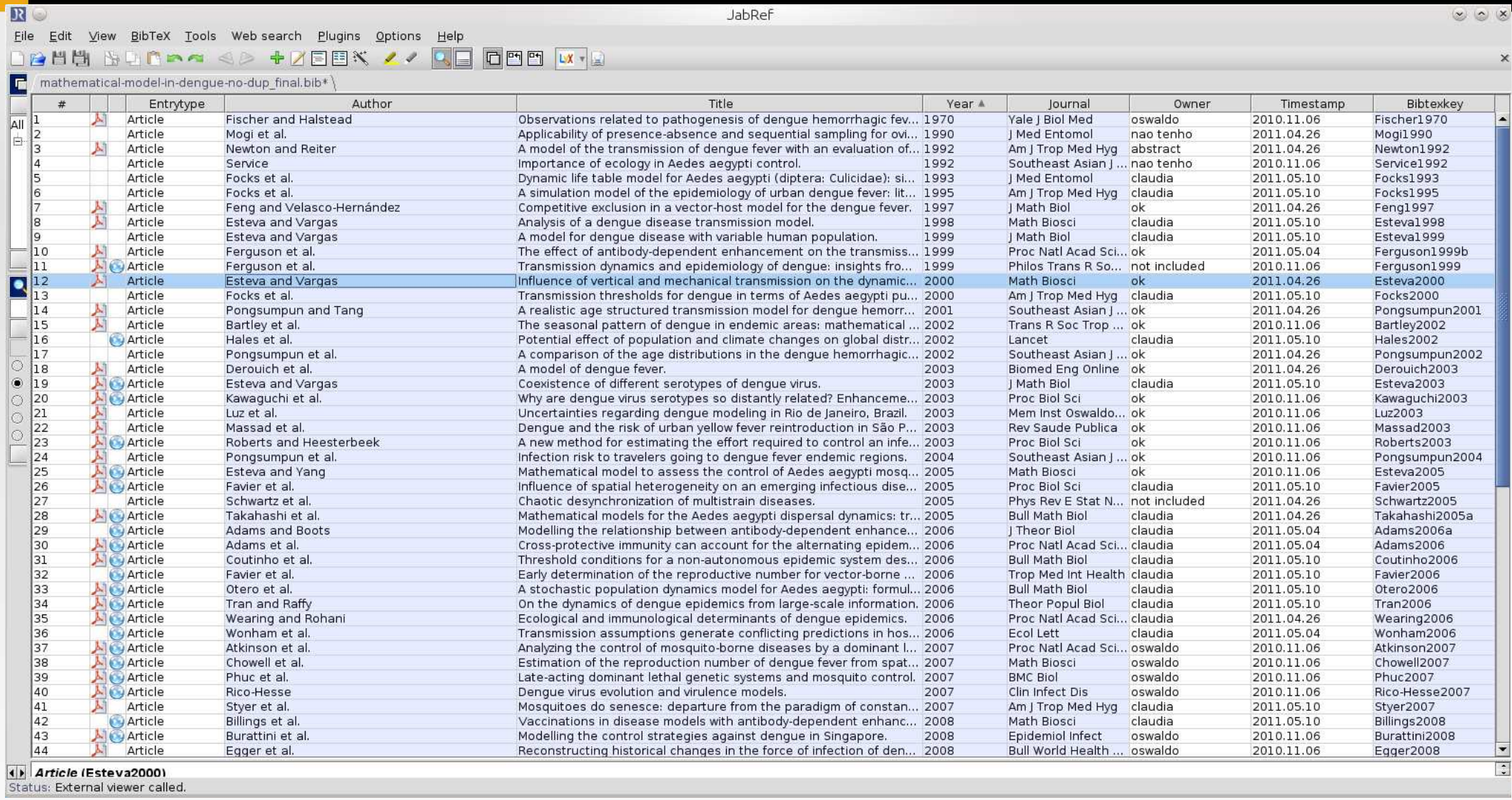
YALE JOURNAL OF BIOLOGY AND MEDICINE *Volume 42, April, 1970*

OBSERVATIONS RELATED TO PATHOGENESIS OF DENGUE HEMORRHAGIC FEVER. V. EXAMINATION OF AGE SPECIFIC SEQUENTIAL INFECTION RATES USING A MATHEMATICAL MODEL†

Calculations were carried out on an IBM 7094 digital computer.

It is the purpose of this paper to utilize the above observations in a study of mathematical models which permit prediction of age specific secondary or tertiary infection rates in populations exposed to three or four different dengue viruses. Results from models have been compared with available epidemiologic data, particularly age specific hemorrhagic fever hospitalization rates, to evaluate hypotheses concerning the number of infections and the interval between infections required to produce DHF.

Base de referências - DSpace



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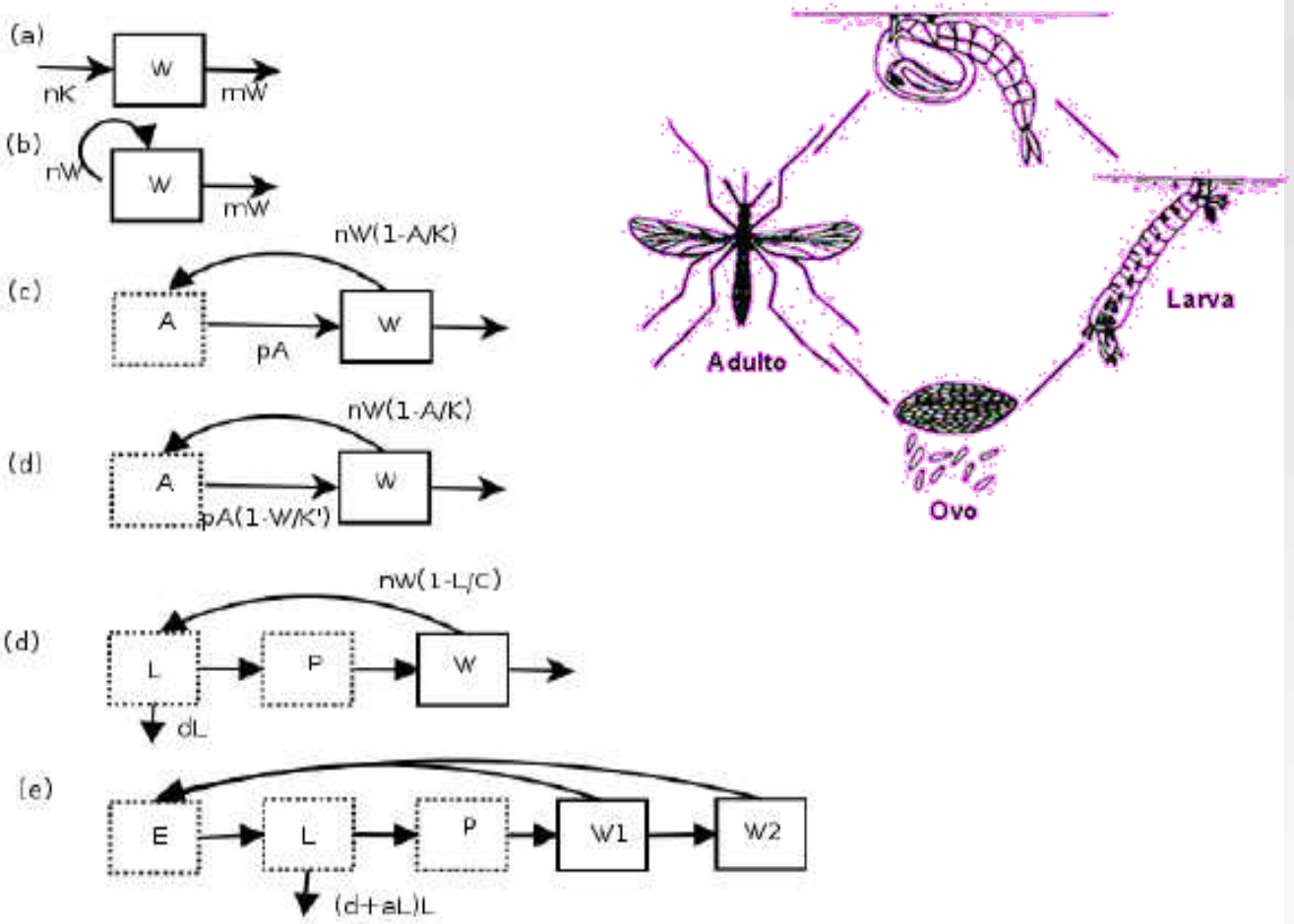
1	Article	Fischer and Halstead	Observations related to pathogenesis of dengue hemorrhagic fev...	1970	Yale J Biol Med	oswaldo	2010.11.06	Fischer1970
2	Article	Mogi et al.	Applicability of presence-absence and sequential sampling for ovi...	1990	J Med Entomol	nao tenho	2011.04.26	Mogi1990
3	Article	Newton and Reiter	A model of the transmission of dengue fever with an evaluation of...	1992	Am J Trop Med Hyg	abstract	2011.04.26	Newton1992
4	Article	Service	Importance of ecology in Aedes aegypti control.	1992	Southeast Asian J ...	nao tenho	2010.11.06	Service1992
5	Article	Focks et al.	Dynamic life table model for Aedes aegypti (diptera: Culicidae): si...	1993	J Med Entomol	claudia	2011.05.10	Focks1993
6	Article	Focks et al.	A simulation model of the epidemiology of urban dengue fever: lit...	1995	Am J Trop Med Hyg	claudia	2011.05.10	Focks1995
7	Article	Feng and Velasco-Hernández	Competitive exclusion in a vector-host model for the dengue fever.	1997	J Math Biol	ok	2011.04.26	Feng1997
8	Article	Esteva and Vargas	Analysis of a dengue disease transmission model.	1998	Math Biosci	claudia	2011.05.10	Esteva1998
9	Article	Esteva and Vargas	A model for dengue disease with variable human population.	1999	J Math Biol	claudia	2011.05.10	Esteva1999
10	Article	Ferguson et al.	The effect of antibody-dependent enhancement on the transmiss...	1999	Proc Natl Acad Sci...	ok	2011.05.04	Ferguson1999b
11	Article	Ferguson et al.	Transmission dynamics and epidemiology of dengue: insights fro...	1999	Philos Trans R So...	not included	2010.11.06	Ferguson1999
12	Article	Esteva and Vargas	Influence of vertical and mechanical transmission on the dynamic...	2000	Math Biosci	ok	2011.04.26	Esteva2000
13	Article	Focks et al.	Transmission thresholds for dengue in terms of Aedes aegypti pu...	2000	Am J Trop Med Hyg	claudia	2011.05.10	Focks2000
14	Article	Pongsumpun and Tang	A realistic age structured transmission model for dengue hemorr...	2001	Southeast Asian J ...	ok	2011.04.26	Pongsumpun2001
15	Article	Bartley et al.	The seasonal pattern of dengue in endemic areas: mathematical ...	2002	Trans R Soc Trop ...	ok	2010.11.06	Bartley2002
16	Article	Hales et al.	Potential effect of population and climate changes on global distr...	2002	Lancet	claudia	2011.05.10	Hales2002
17	Article	Pongsumpun et al.	A comparison of the age distributions in the dengue hemorrhagic...	2002	Southeast Asian J ...	ok	2011.04.26	Pongsumpun2002
18	Article	Derouich et al.	A model of dengue fever.	2003	Biomed Eng Online	ok	2011.04.26	Derouich2003
19	Article	Esteva and Vargas	Coexistence of different serotypes of dengue virus.	2003	J Math Biol	claudia	2011.05.10	Esteva2003
20	Article	Kawaguchi et al.	Why are dengue virus serotypes so distantly related? Enhanceme...	2003	Proc Biol Sci	ok	2010.11.06	Kawaguchi2003
21	Article	Luz et al.	Uncertainties regarding dengue modeling in Rio de Janeiro, Brazil.	2003	Mem Inst Oswaldo...	ok	2010.11.06	Luz2003
22	Article	Massad et al.	Dengue and the risk of urban yellow fever reintroduction in São P...	2003	Rev Saude Publica	ok	2010.11.06	Massad2003
23	Article	Roberts and Heesterbeek	A new method for estimating the effort required to control an infe...	2003	Proc Biol Sci	ok	2010.11.06	Roberts2003
24	Article	Pongsumpun et al.	Infection risk to travelers going to dengue fever endemic regions.	2004	Southeast Asian J ...	ok	2010.11.06	Pongsumpun2004
25	Article	Esteva and Yang	Mathematical model to assess the control of Aedes aegypti mosq...	2005	Math Biosci	ok	2010.11.06	Esteva2005
26	Article	Favier et al.	Influence of spatial heterogeneity on an emerging infectious dise...	2005	Proc Biol Sci	claudia	2011.05.10	Favier2005
27	Article	Schwartz et al.	Chaotic desynchronization of multistrain diseases.	2005	Phys Rev E Stat N...	not included	2011.04.26	Schwartz2005
28	Article	Takahashi et al.	Mathematical models for the Aedes aegypti dispersal dynamics: tr...	2005	Bull Math Biol	claudia	2011.04.26	Takahashi2005a
29	Article	Adams and Boots	Modelling the relationship between antibody-dependent enhance...	2006	J Theor Biol	claudia	2011.05.04	Adams2006a
30	Article	Adams et al.	Cross-protective immunity can account for the alternating epidem...	2006	Proc Natl Acad Sci...	claudia	2011.05.04	Adams2006
31	Article	Coutinho et al.	Threshold conditions for a non-autonomous epidemic system des...	2006	Bull Math Biol	claudia	2011.05.10	Coutinho2006
32	Article	Favier et al.	Early determination of the reproductive number for vector-borne ...	2006	Trop Med Int Health	claudia	2011.05.10	Favier2006
33	Article	Otero et al.	A stochastic population dynamics model for Aedes aegypti: formul...	2006	Bull Math Biol	claudia	2011.05.10	Otero2006
34	Article	Tran and Raffy	On the dynamics of dengue epidemics from large-scale information.	2006	Theor Popul Biol	claudia	2011.05.10	Tran2006
35	Article	Wearing and Rohani	Ecological and immunological determinants of dengue epidemics.	2006	Proc Natl Acad Sci...	claudia	2011.04.26	Wearing2006
36	Article	Wonham et al.	Transmission assumptions generate conflicting predictions in hos...	2006	Ecol Lett	claudia	2011.05.04	Wonham2006
37	Article	Atkinson et al.	Analyzing the control of mosquito-borne diseases by a dominant l...	2007	Proc Natl Acad Sci...	oswaldo	2010.11.06	Atkinson2007
38	Article	Chowell et al.	Estimation of the reproduction number of dengue fever from spat...	2007	Math Biosci	oswaldo	2010.11.06	Chowell2007
39	Article	Phuc et al.	Late-acting dominant lethal genetic systems and mosquito control.	2007	BMC Biol	oswaldo	2010.11.06	Phuc2007
40	Article	Rico-Hesse	Dengue virus evolution and virulence models.	2007	Clin Infect Dis	oswaldo	2010.11.06	Rico-Hesse2007
41	Article	Styer et al.	Mosquitoes do senesce: departure from the paradigm of constan...	2007	Am J Trop Med Hyg	claudia	2011.05.10	Styer2007
42	Article	Billings et al.	Vaccinations in disease models with antibody-dependent enhanc...	2008	Math Biosci	claudia	2011.05.10	Billings2008
43	Article	Burattini et al.	Modelling the control strategies against dengue in Singapore.	2008	Epidemiol Infect	oswaldo	2010.11.06	Burattini2008
44	Article	Egger et al.	Reconstructing historical changes in the force of infection of den...	2008	Bull World Health ...	oswaldo	2010.11.06	Egger2008

Deconstructing dengue models

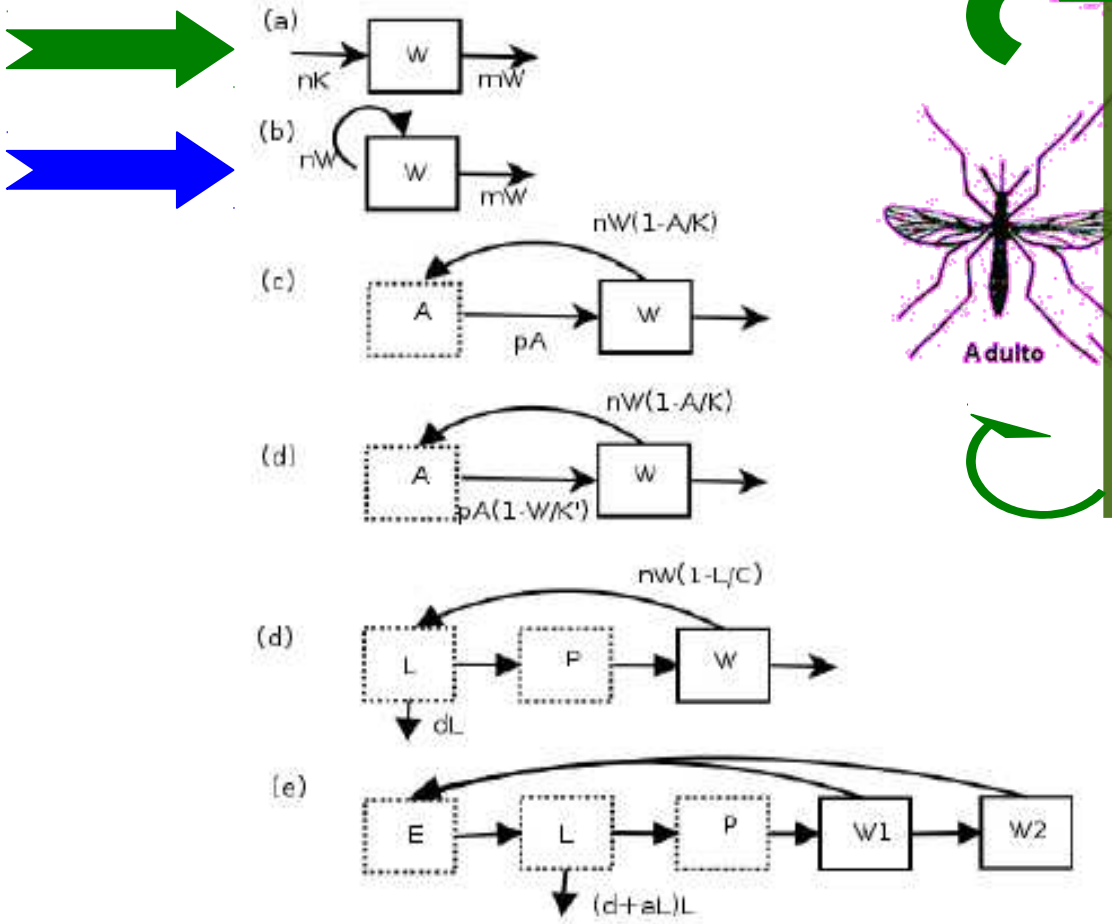
Figura 1: Schematic models for the Aedes aegypti vital dynamics

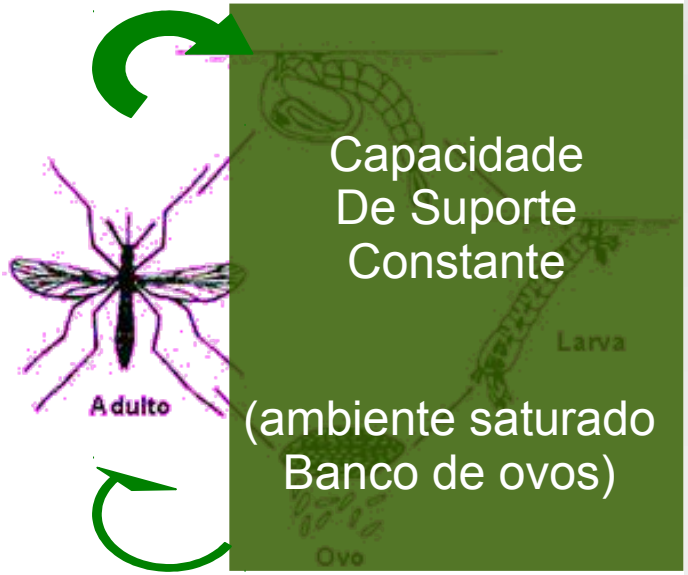


ente não
retem nada)

Modelo caixa preta

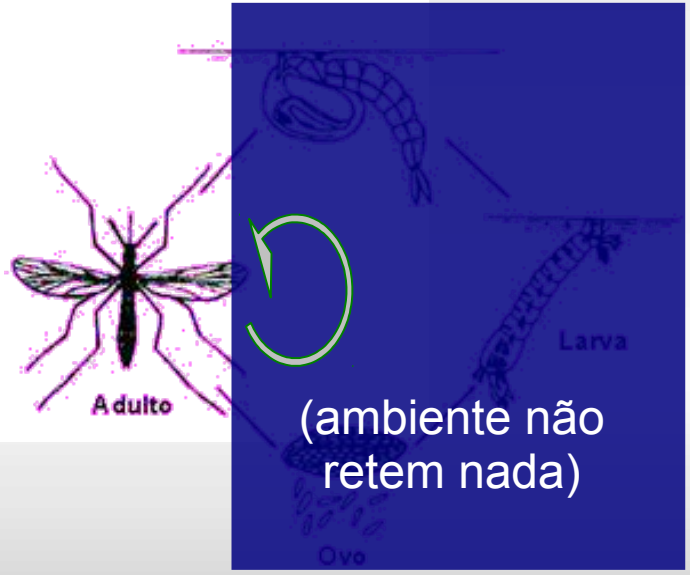
Figura 1: Schematic models for the Aedes aegypti vital dynamics





Capacidade
De Suporte
Constante

(ambiente saturado
Banco de ovos)

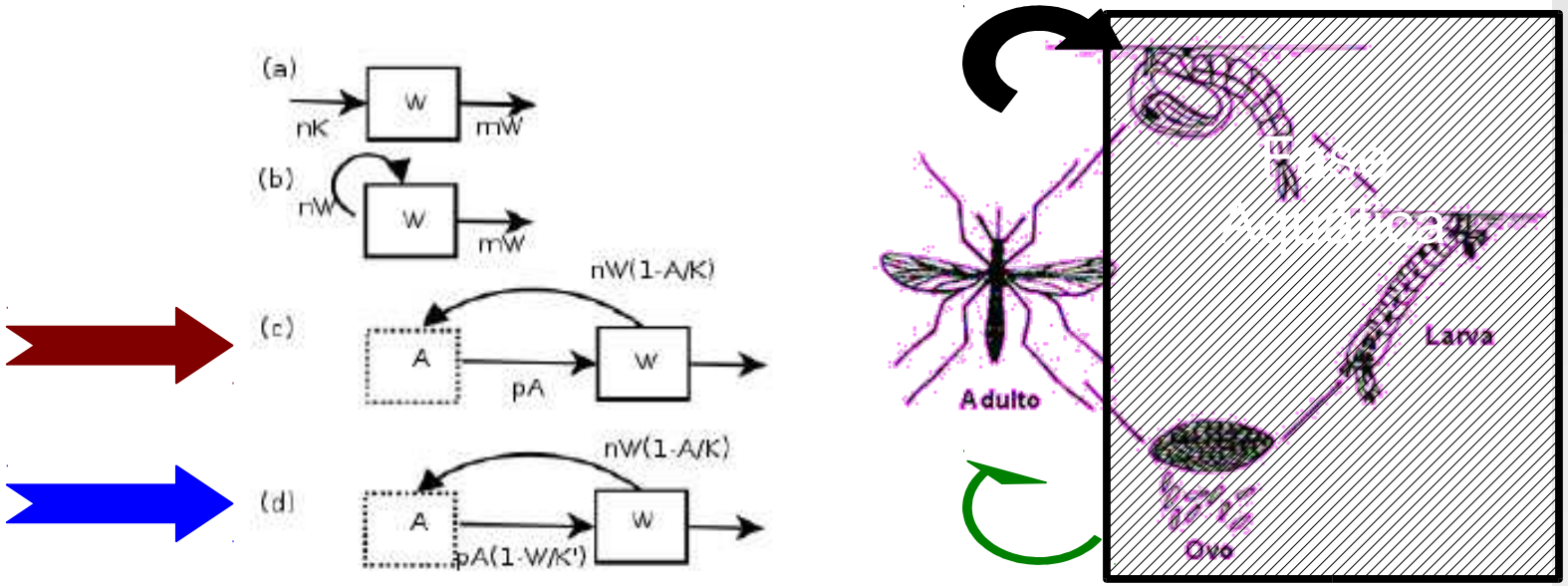


(ambiente não
retem nada)

Predições diferentes para o impacto de estratégias que visam
O adulto e que visam a remoção de ovos

Modelo caixa cinza

Figura 1: Schematic models for the Aedes aegypti vital dynamics



Pressupostos:

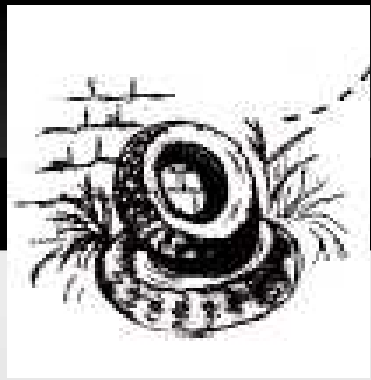
- Oviposição dependente da densidade

- Emergência independente da densidade de larvas

- Emergência dependente da densidade de adultos

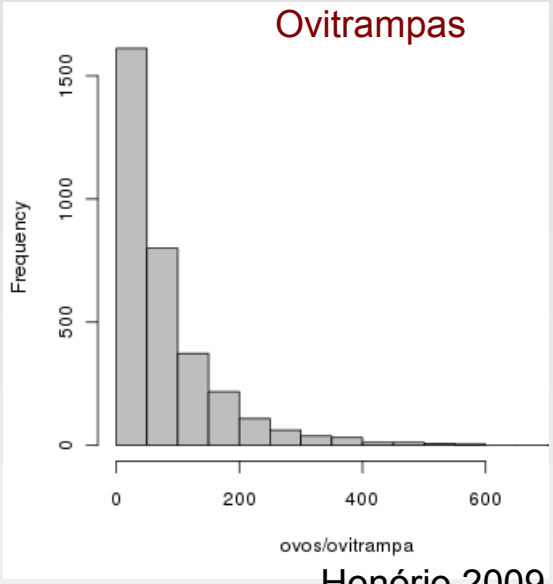
- Implícito: Ausência de um banco de ovos (fase de vida latente)

Oviposição dependente da densidade?



(1) Dados de ovitrampas não parecem indicar efeito inibitório dos ovos presentes.

Ovitrampas



Honório 2009

Ovitrampas grandes

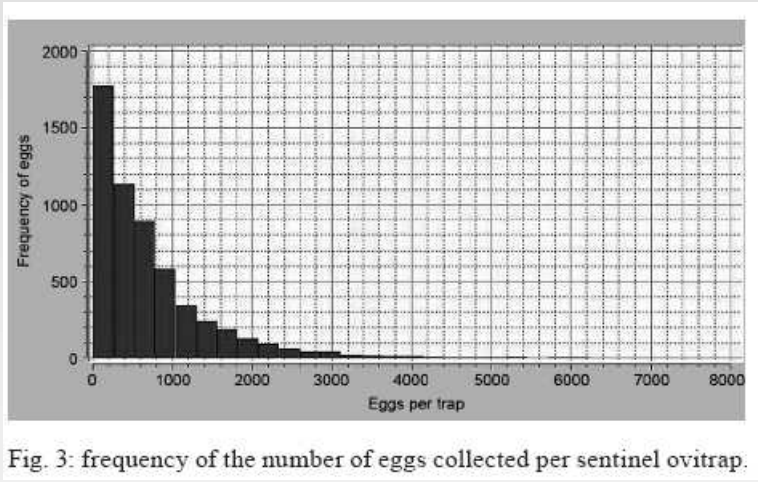


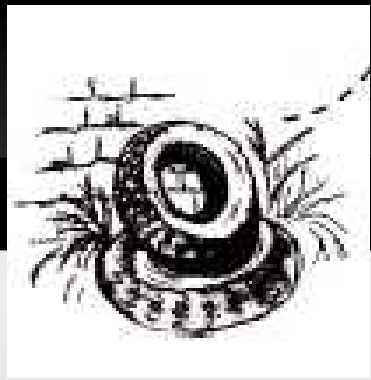
Fig. 3: frequency of the number of eggs collected per sentinel ovitrap.

Regis et al, 2008

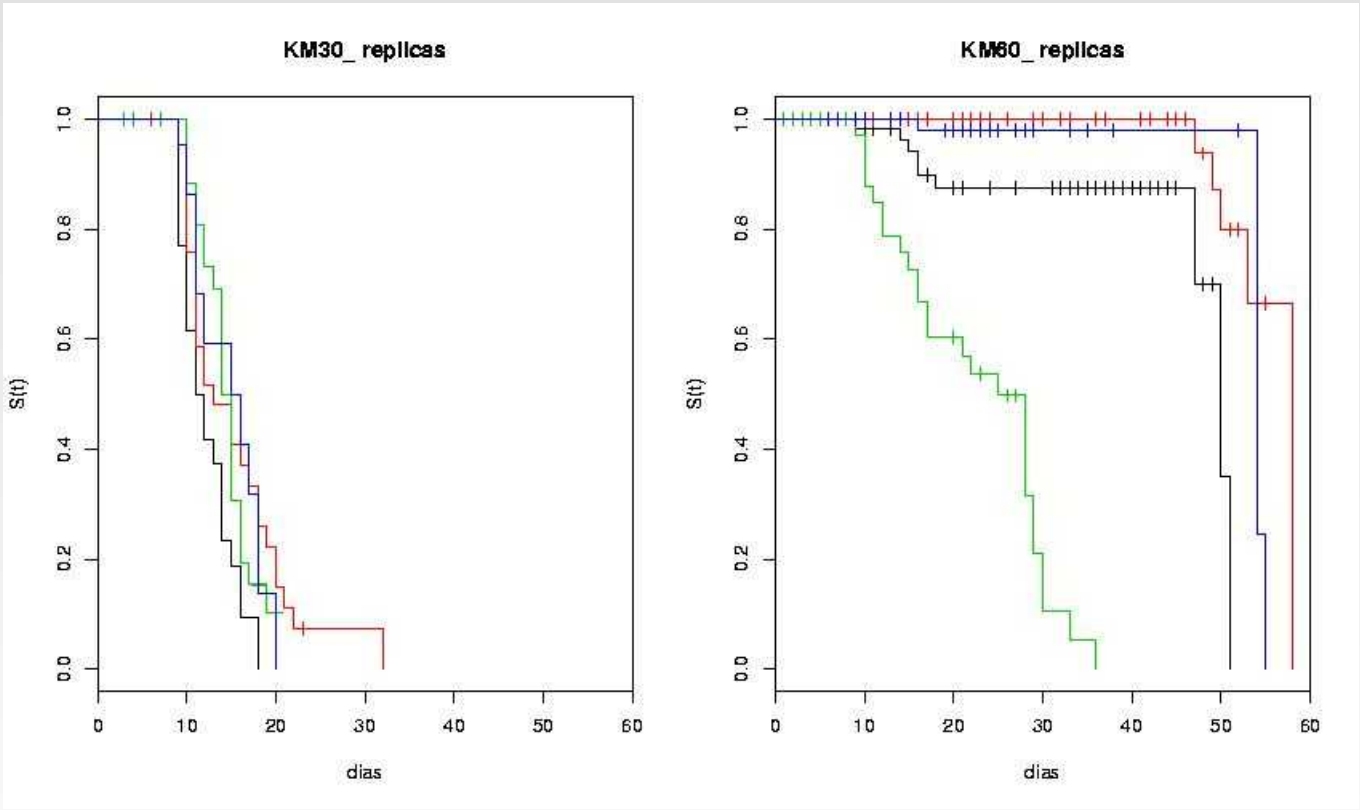
(2) Estudos comportamentais sugerem efeito estimulante da presença de larvas, Mas e se houverem muitas?

- Fêmeas poderiam reter os ovos caso já houvessem muitas larvas?

Emergência dependente da densidade?



(1) Sim! Curvas de sobrevida de tempo até pupamento

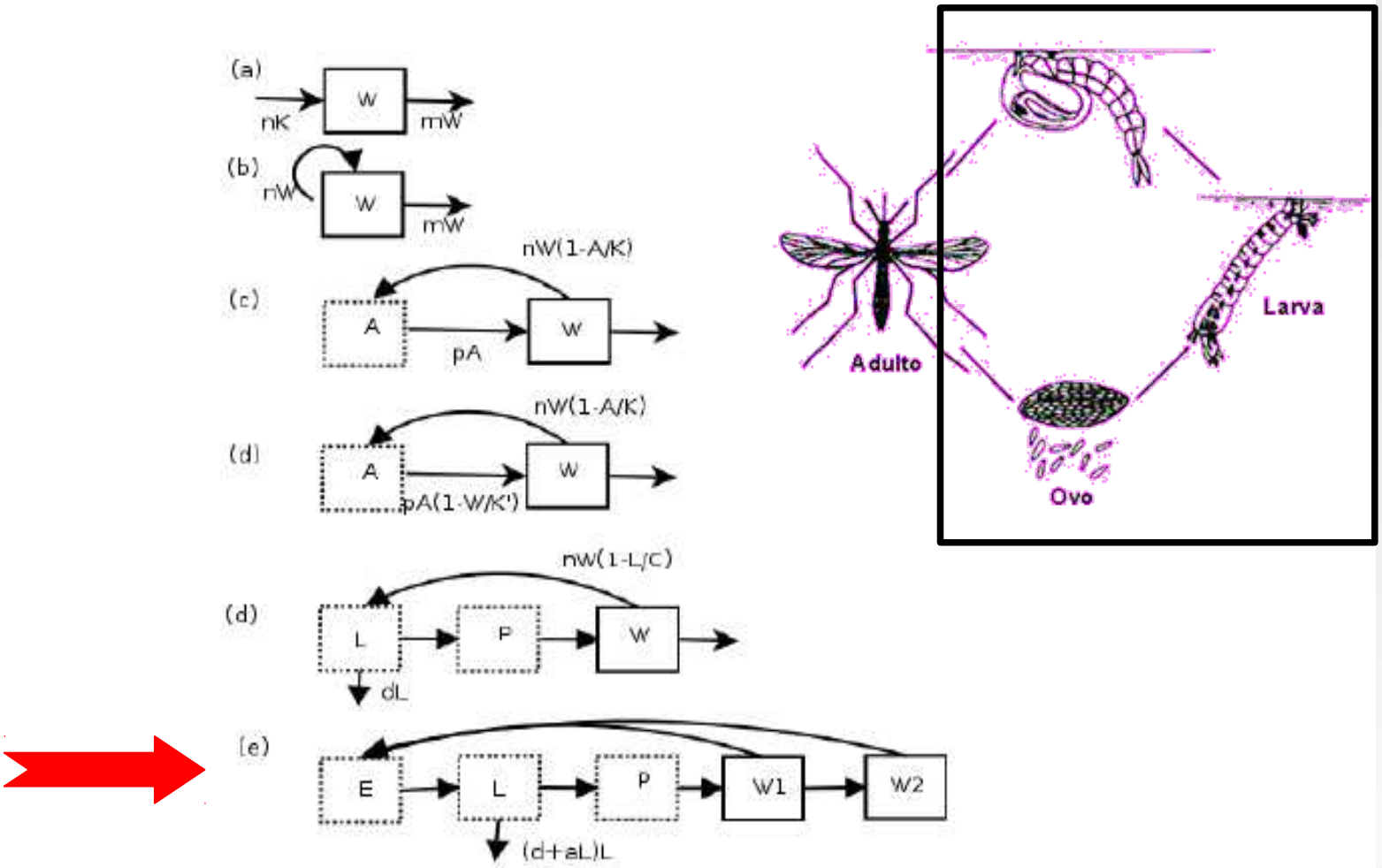


Baixa densidade

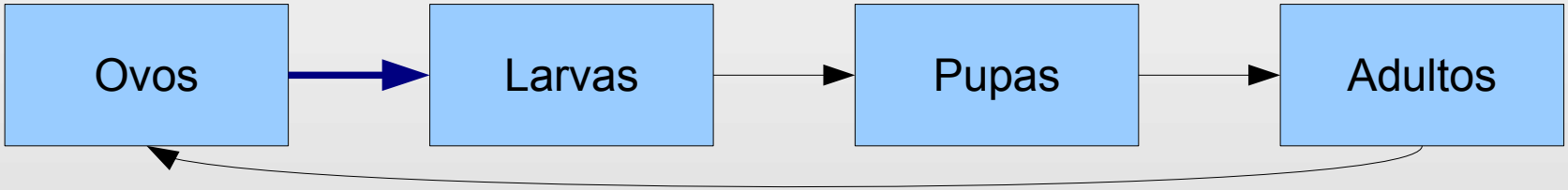
Alta densidade

Modelo caixa branca

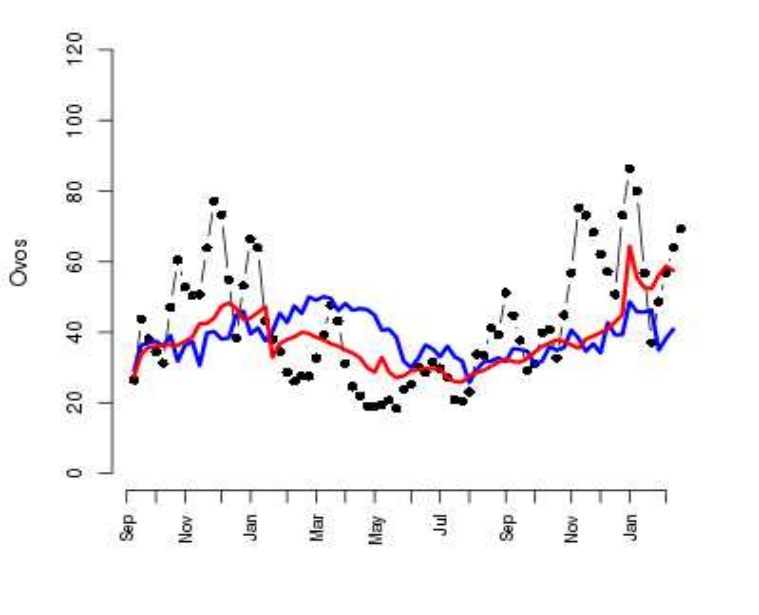
Figura 1: Schematic models for the Aedes aegypti vital dynamics

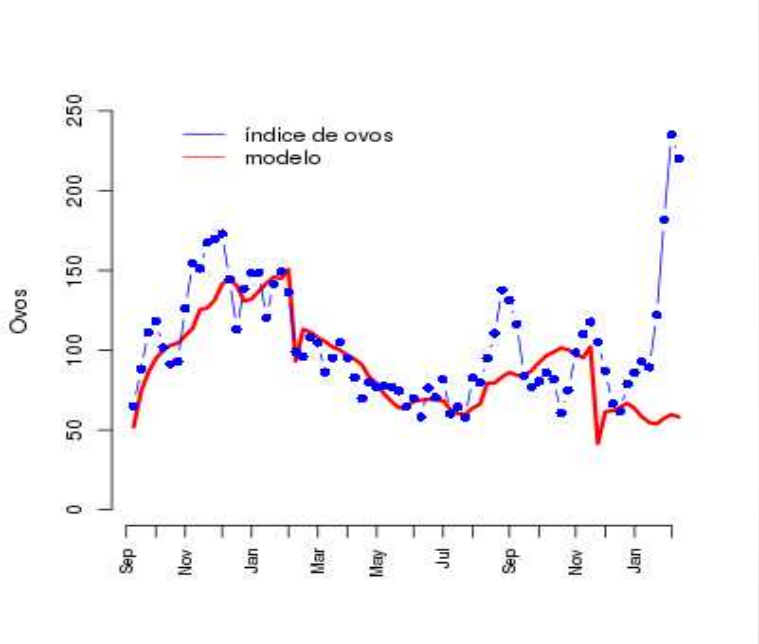


Modelo caixa branca

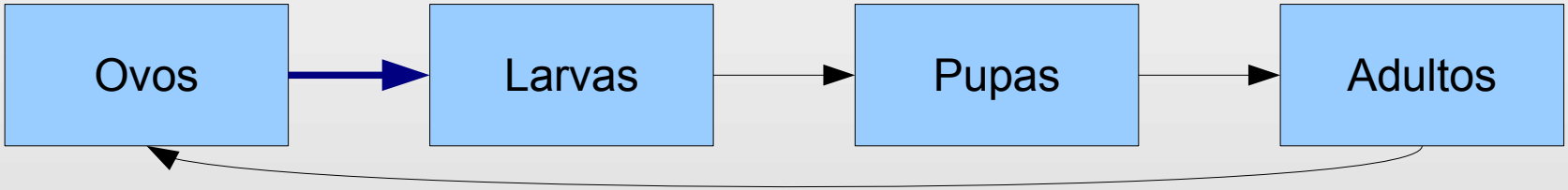


- dependência da densidade (oviposição e pupação)
- efeito da temperatura
- capacidade de suporte no verão ≠ inverno





Modelo caixa branca



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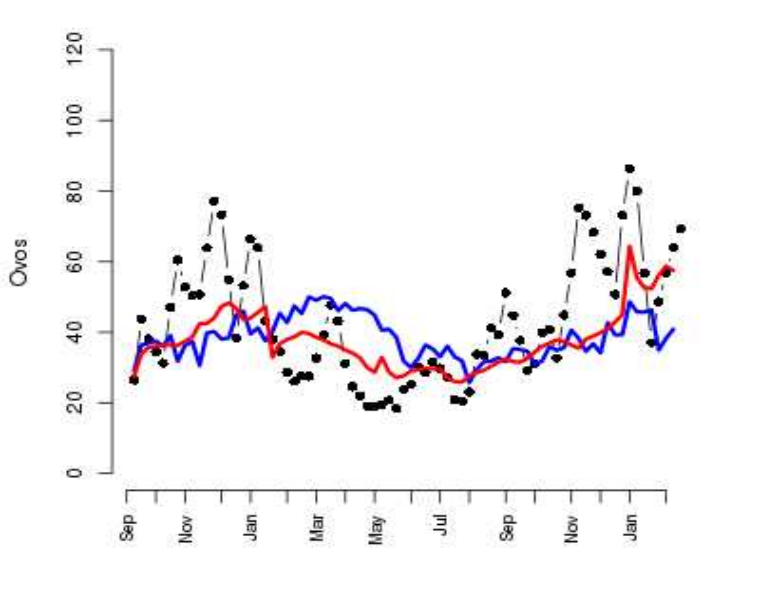
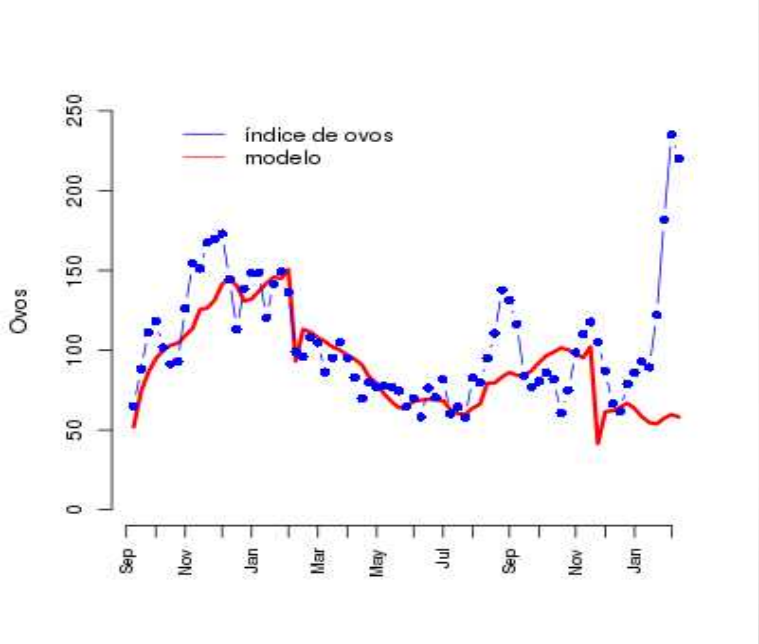




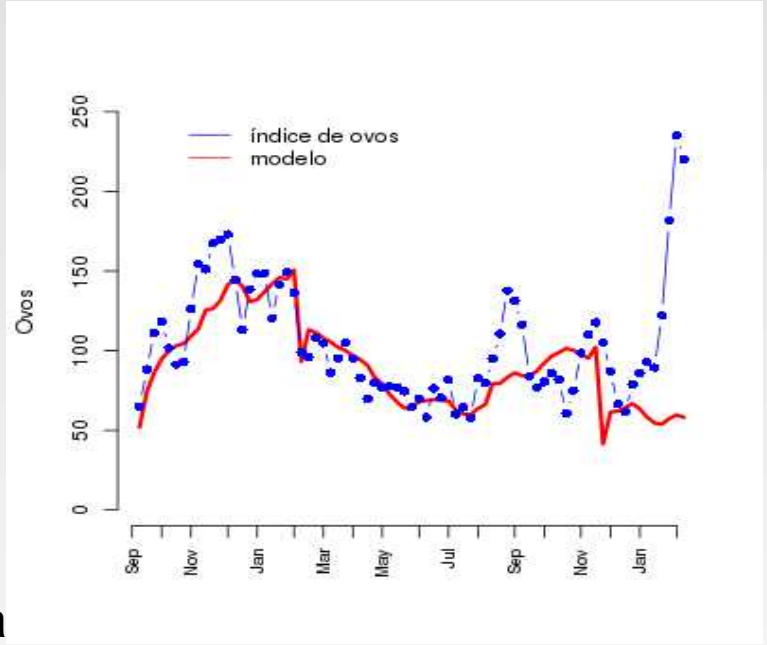
Verdade??

Proposição: Um ovo pode eclodir em 2 dias
Um ovo pode viver 7 meses ou mais

O que determina a eclosão não é um relógio Fisiológico mas o ambiente.

Estocasticidade vs Determinismo

Se condições propícias são raras, então a
Dinâmica é oportunística e depende do ambiente
Eventos serão estocásticos
E abruptos



Se o ambiente é propício, então a dinâmica se aproxima
Relógio endógeno, e eventos são mais suaves e a dinâmica
Mais previsivel.

Minha wishlist

- De forma quantitativa, qual o efeito na oviposição, da densidade de larvas e ovos?

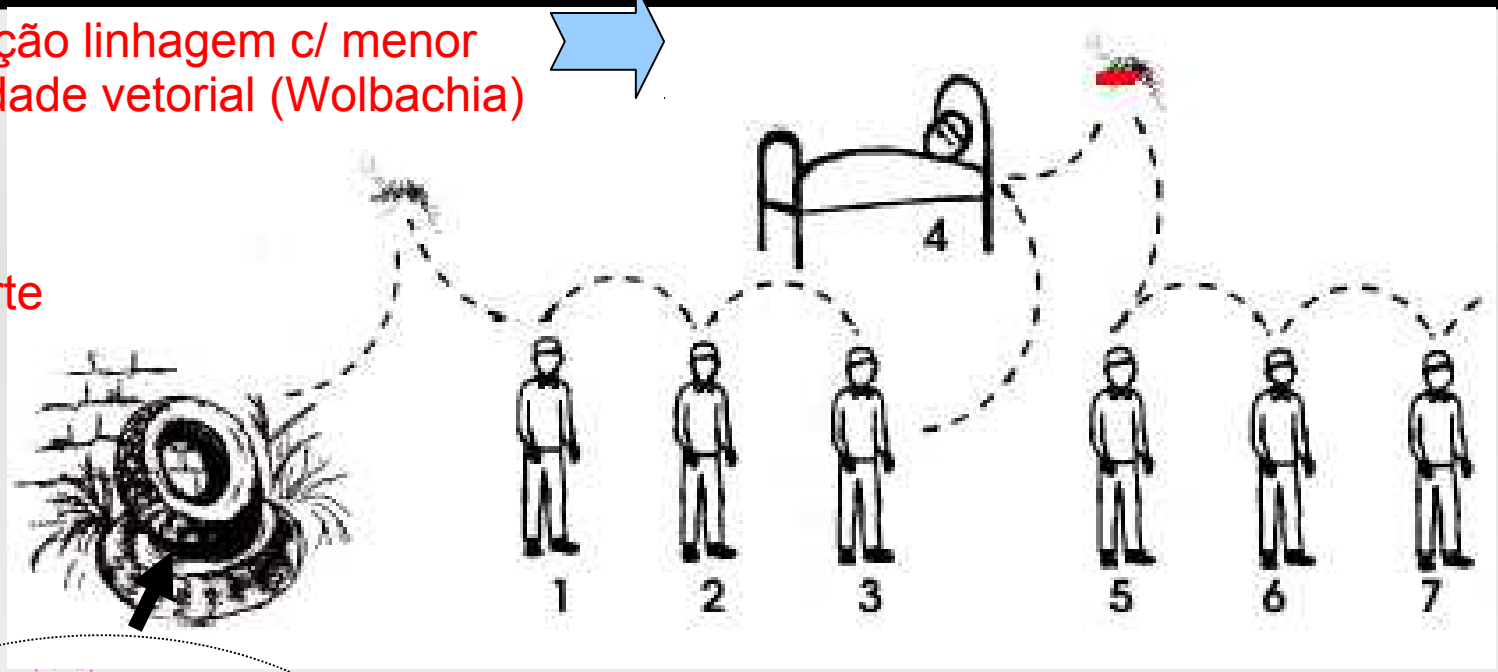
- De forma quantitativa, como é a dinâmica de eclosão dos ovos? Qual o efeito do ambiente na taxa de eclosão?

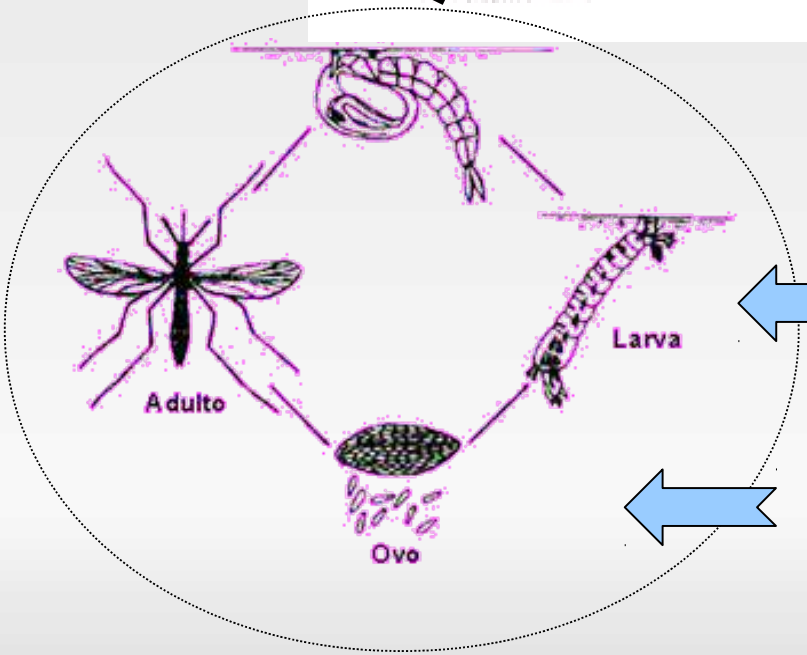
- Existe evidência de esgotamento de ovos no ambiente? Em que condições pode ocorrer?

Obrigada!

Introdução linhagem c/ menor capacidade vetorial (Wolbachia)

Redução da Capacidade de suporte





larvicidas

Remoção intensiva de ovos (inundação De armadilhas)

Introdução Machos estéreis