MATHEMATICAL FRONTIERS

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Board on
Mathematical Sciences & Analytics

MATHEMATICAL FRONTIERS
2018 Monthly Webinar Series, 2-3pm ET

February 13*:
Mathematics of the Electric Grid

March 13*:
Probability for People and Places

April 10*:
Social and Biological Networks

May 8*:
Mathematics of Redistricting

June 12*: *Number Theory: The Riemann Hypothesis*

July 10*: *Topology*

August 14*: *Algorithms for Threat Detection*

September 11*: *Mathematical Analysis*

October 9*: *Combinatorics*

November 13*:
Why Machine Learning Works

December 11:
Mathematics of Epidemics

*** *Recording posted***

Made possible by support for BMSA from the National Science Foundation Division of Mathematical Sciences and the Department of Energy Advanced Scientific Computing Research

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MATHEMATICAL FRONTIERS

2019 Monthly Webinar Series, 2-3pm ET

February 12: *Machine Learning for Materials Science and Drug Discovery*

March 12: *Mathematics of Privacy*

April 9: *Mathematics in Astronomy*

May 14: *Algebraic Geometry*

June 11: *Transportation and Urban Planning*

July 9: *Cryptography and Cybersecurity*

August 13: *Machine Learning for Genomics and Medicine*

September 10: *Logic and Foundations*

October 8: *Quantum Physics and String Theory*

November 12: *Quantum Encryption*

December 10: *Machine Learning and Text*

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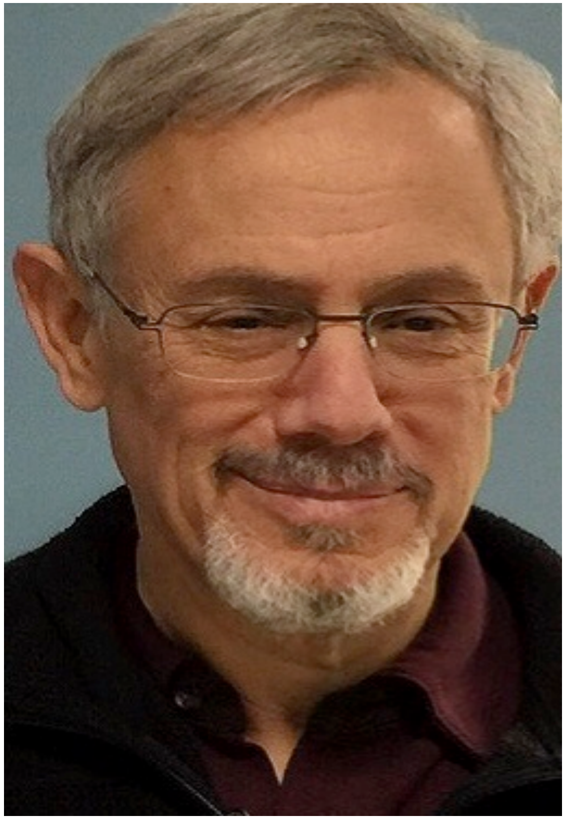
MATHEMATICAL FRONTIERS

Mathematics of Epidemics



Folashade Agusto,
University of Kansas

Calistus Ngonghala,
University of Florida, Gainesville

Mark Green,
UCLA (moderator)

View webinar videos and learn more about BMSA at www.nas.edu/MathFrontiers

Folashade Agusto,
University of Kansas

Assistant Professor
Ecology and Evolutionary Biology
University of Kansas

Strategies for disease and infestation control

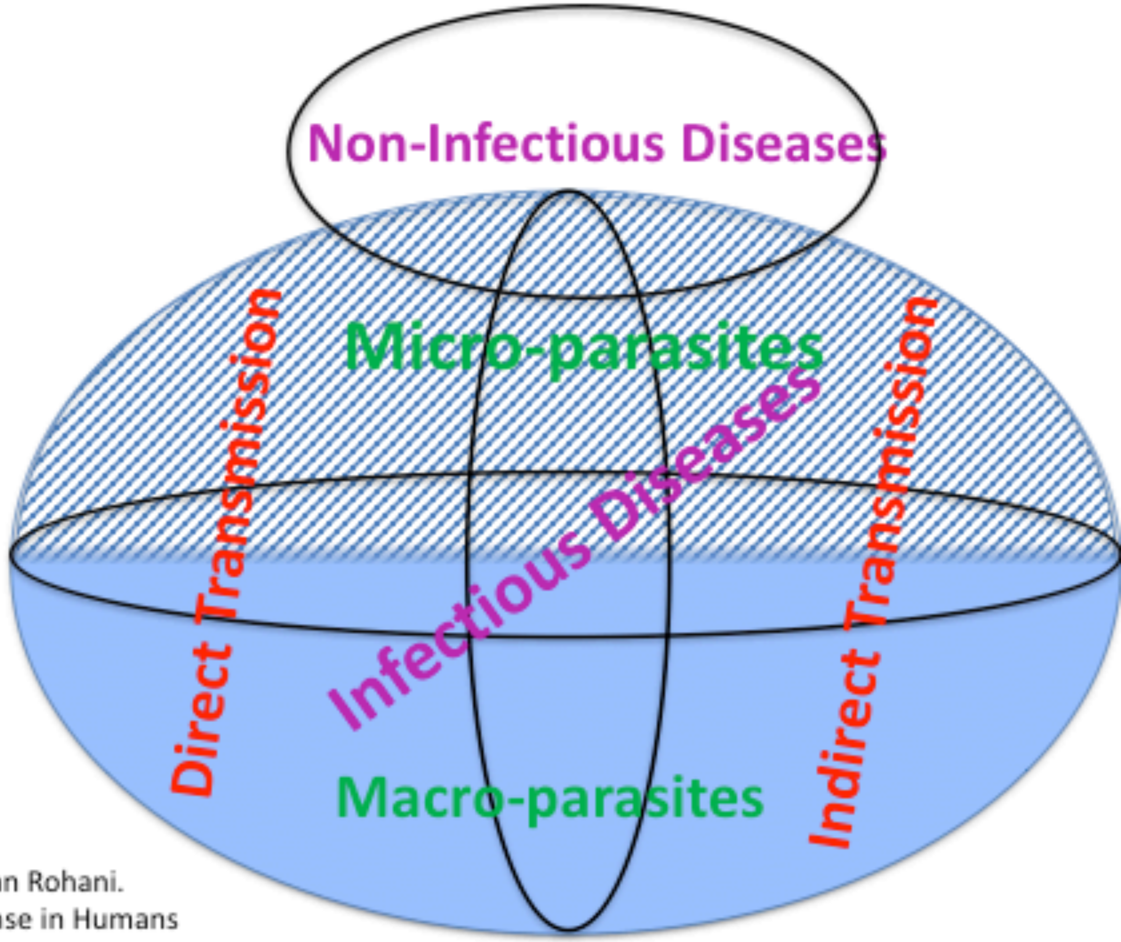
Classification of Diseases

What is disease?

This is a condition of the body, or of some parts or organs of the body, which interrupt the body's regular function.

Examples:

AIDS, arthritis, common cold, cancer, Bovine TB, malaria, Ebola, Zika etc.



Matt J. Keeling and Pejman Rohani. Modeling Infectious Disease in Humans and Animals. Princeton University Press 2008.

Why do we model infectious diseases?

1. Gain insight into mechanisms influencing disease spread, and to link the individual scale 'clinical' knowledge with population-scale patterns.

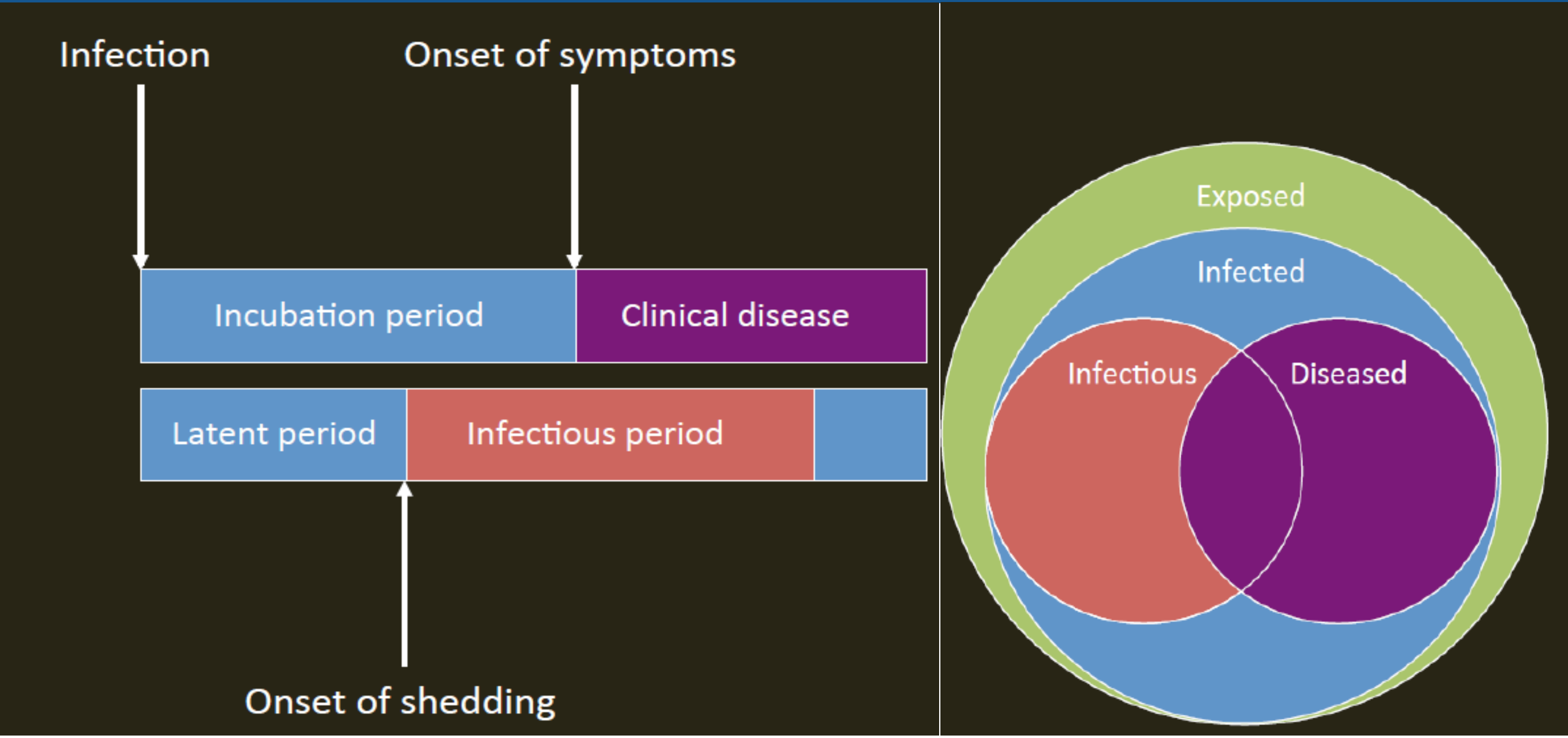
2. Derive new insights and hypotheses from mathematical analysis or simulation.

3. Establish relative importance of different processes and parameters, to focus research or management effort.

4. To address *via* thought experiments the "what if" questions, since real experiments are often logistically or ethically impossible.

5. Explore management options.

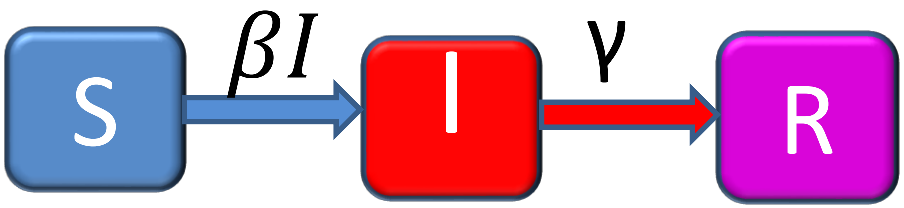
Natural History of Infection



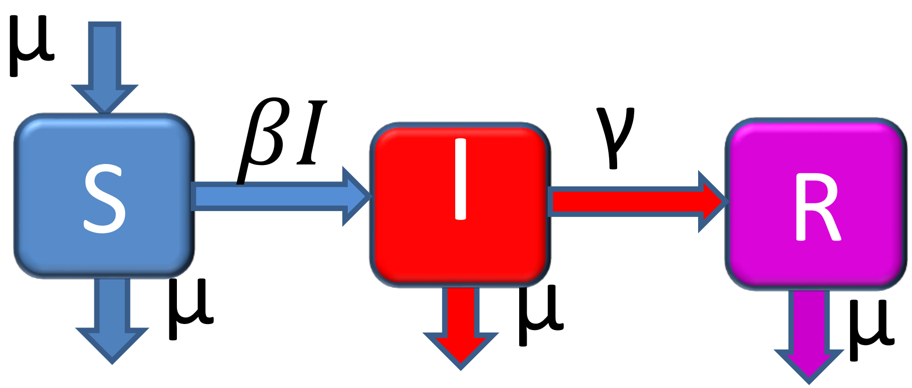
Steve Bellan Introduction to Infectious Disease Modelling Clinic on the Meaningful Modeling of Epidemiological Data, (2015)
African Institute for Mathematical Sciences Muizenberg, South Africa.

Compartmental Disease Models

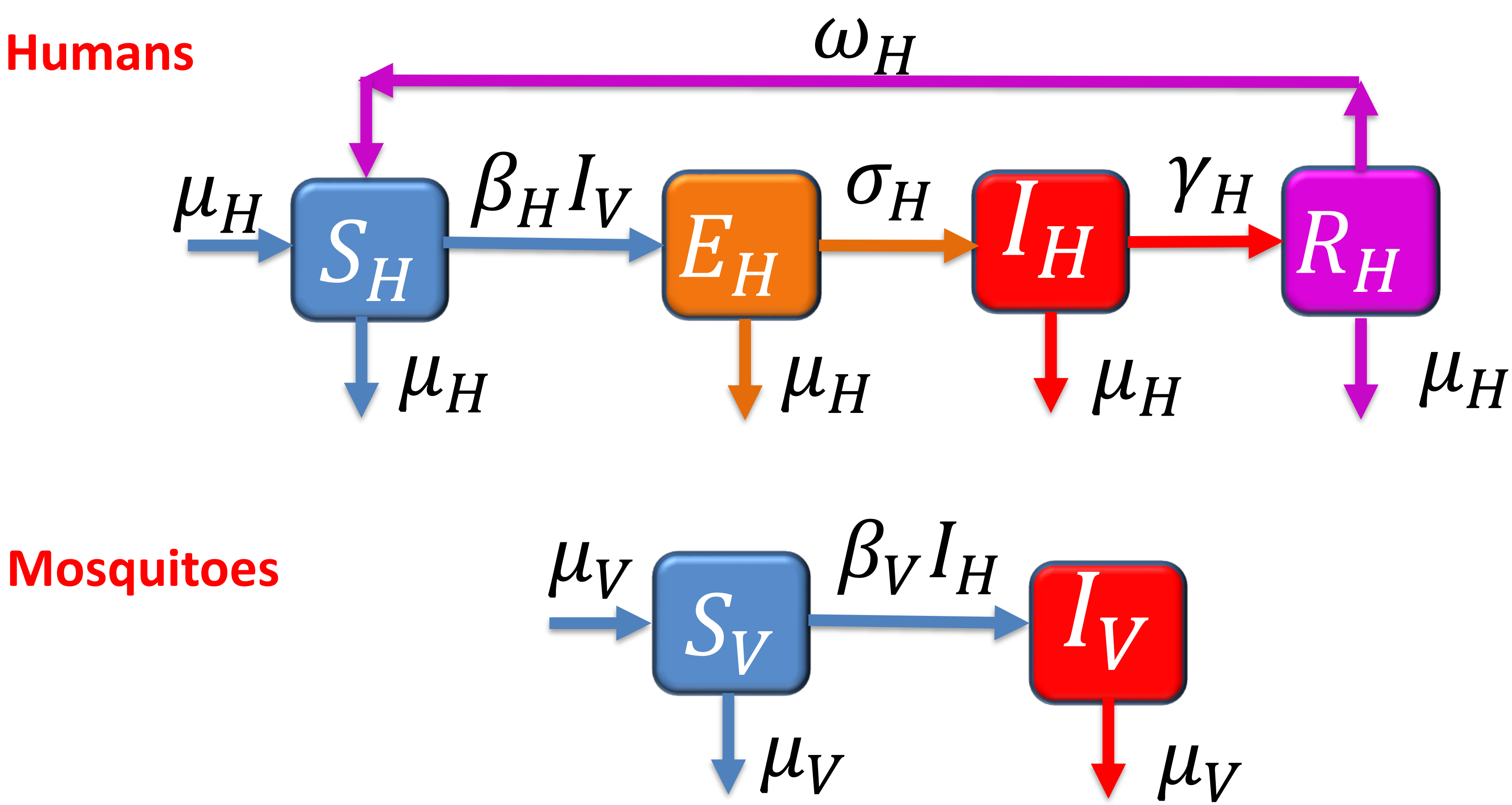
Without demography



With demography



Compartmental Disease Models



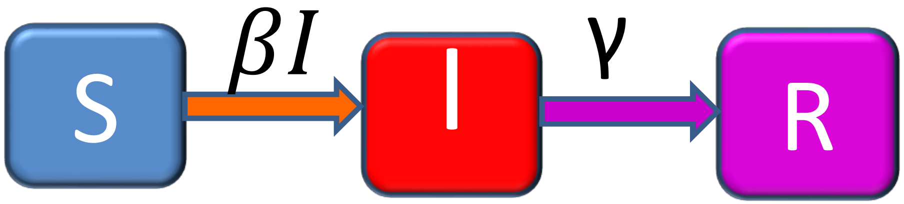
Types of Models

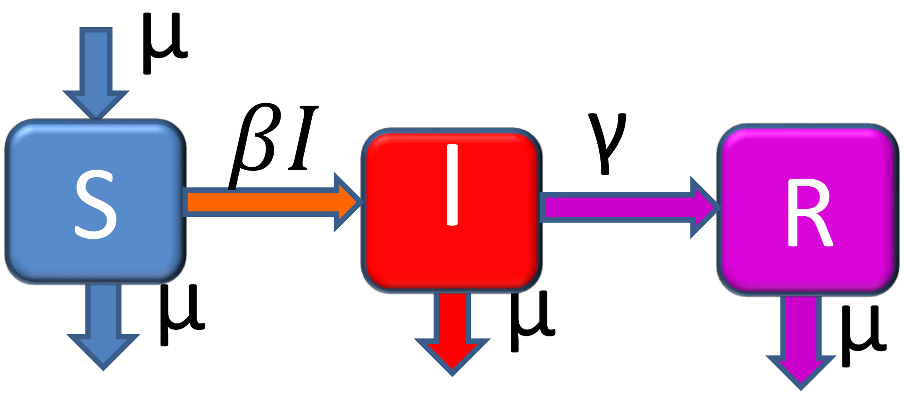
Even after compartmental framework is chosen, still need to decide:

- Deterministic vs stochastic
- Discrete vs continuous time
- Discrete vs continuous state variables
- Random mixing vs structured population
- Homogeneous vs heterogeneous

  (and which heterogeneities to include?)

Compartmental Disease Models





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

$$\frac{dS}{dt} = \mu - \beta SI - \mu S$$
$$\frac{dI}{dt} = \beta SI - \gamma I - \mu I$$
$$\frac{dR}{dt} = \gamma I - \mu R$$

With initial conditions
$S(0) > 0, I(0) > 0$, and $R(0) = 0$.

Basic reproductive number, R_0

What are the conditions for
- Disease elimination?
- Disease persistence?

These conditions can be determined from the basic reproductive number, R_0

R_0 : The average number of secondary cases caused by a typical infectious individual in a totally susceptible population.

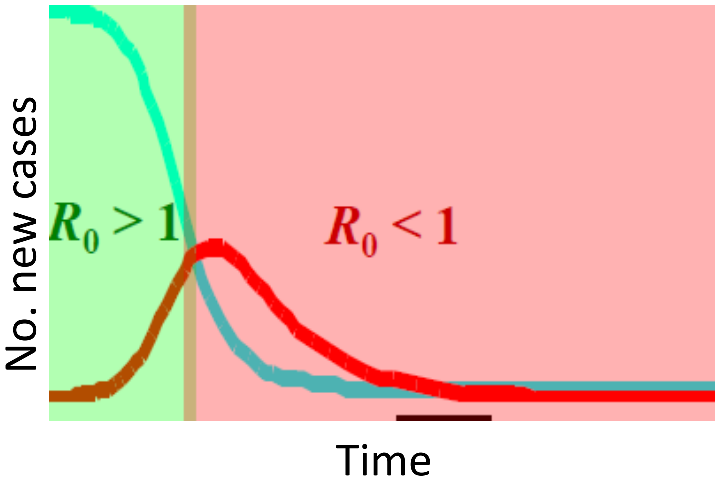
The value of R_0 for some well-known diseases	
Disease	**R_0**
AIDS	2 to 5
Smallpox	3 to 5
Measles	16 to 18
Malaria	> 100

Matthew Keeling
The mathematics of diseases
https://plus.maths.org/content/os/issue14/features/diseases/index

Basic reproductive number, R_0

$R_0 \leq 1$

disease dies out



$R_0 > 1$

disease can invade

Outbreak dynamics

- probability of fade-out
- epidemic growth rate

Disease control

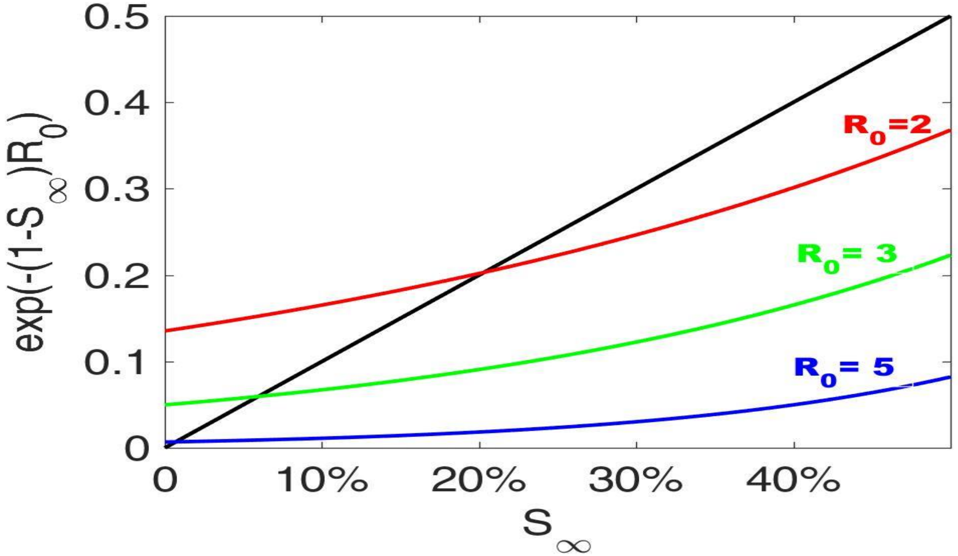
- threshold targets
- vaccination levels

Jamie Lloyd-Smith
Introduction to infectious diseases
Center for Infectious Disease Dynamics, Pennsylvania State University

What does R_0 tell you?

- Probability of successful invasion
- Initial rate of epidemic growth
- Prevalence at the peak of the epidemic
- The proportion of susceptible who would escape the infection (or final epidemic size)

$$S(\infty) = \exp(-(1 - S(\infty)R_0))$$



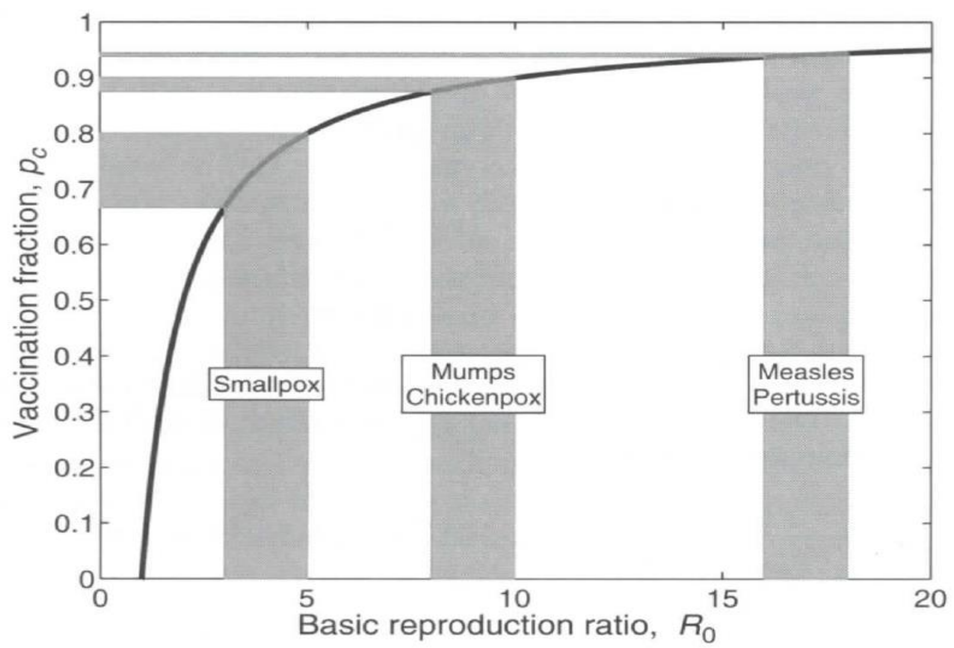
Matt J. Keeling and Pejman Rohani. Modeling Infectious Disease in Humans and Animals. Princeton University Press 2008.

What does R_0 tell you?

- Critical vaccination threshold for eradication

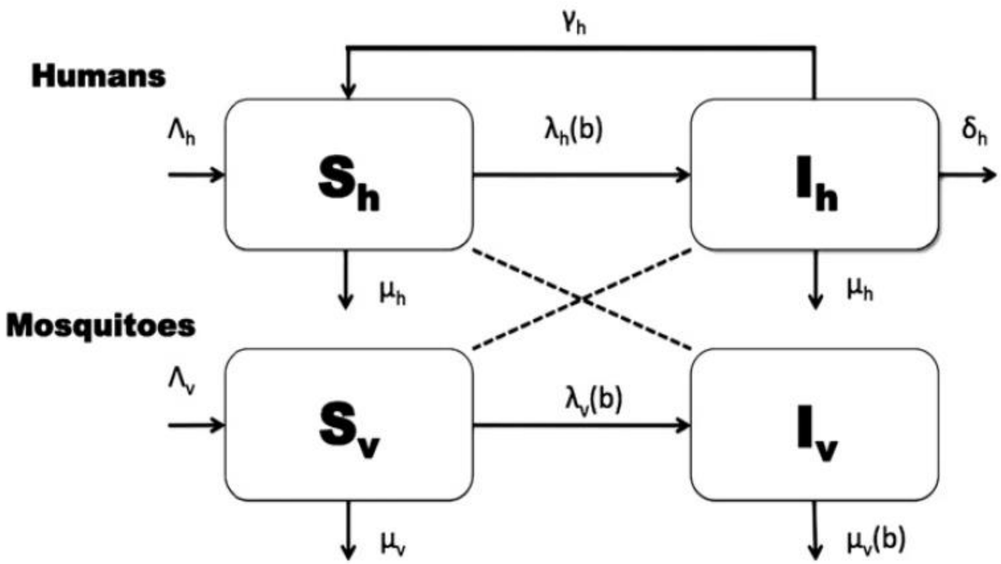
$$P_c = 1 - 1/R_0$$

- Threshold values for other control measures



Matt J. Keeling and Pejman Rohani. Modeling Infectious Disease in Humans and Animals. Princeton University Pres 2008.

The impact of bed-net use on malaria prevalence



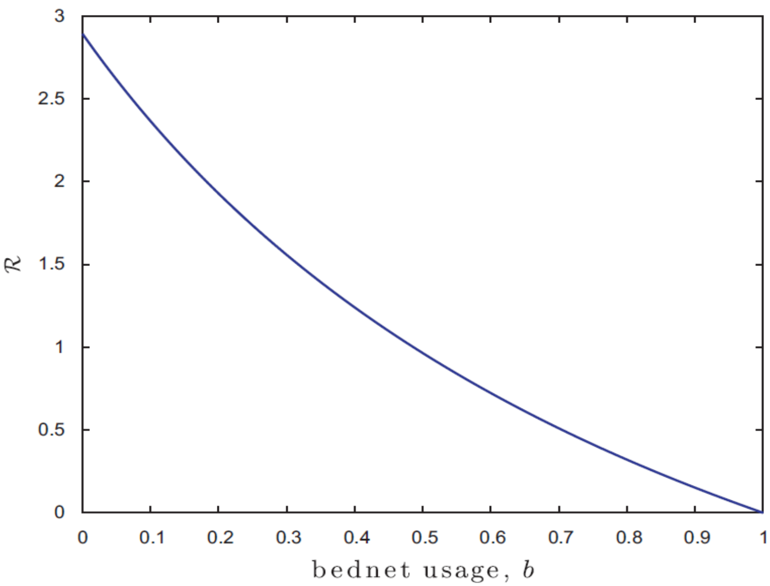
$$\lambda_h(b) = \frac{p_1 \beta(b) I_V}{N_h} \qquad \lambda_v(b) = \frac{p_2 \beta(b) I_h}{N_h}$$

$$\beta(b) = \beta_{\max} - b(\beta_{\max} - \beta_{\min}),$$

$$0 \le b \le 1 \qquad \mu_v(b) = \mu_{v1} + \mu_{v2}(b)$$

Agusto, F. B., Del Valle, S. Y., Blayneh, K. W., Ngonghala, C. N., Goncalves, M. J., Li, N., ... & Gong, H. (2013). The impact of bed-net use on malaria prevalence. *Journal of theoretical biology*, *320*, 58-65.

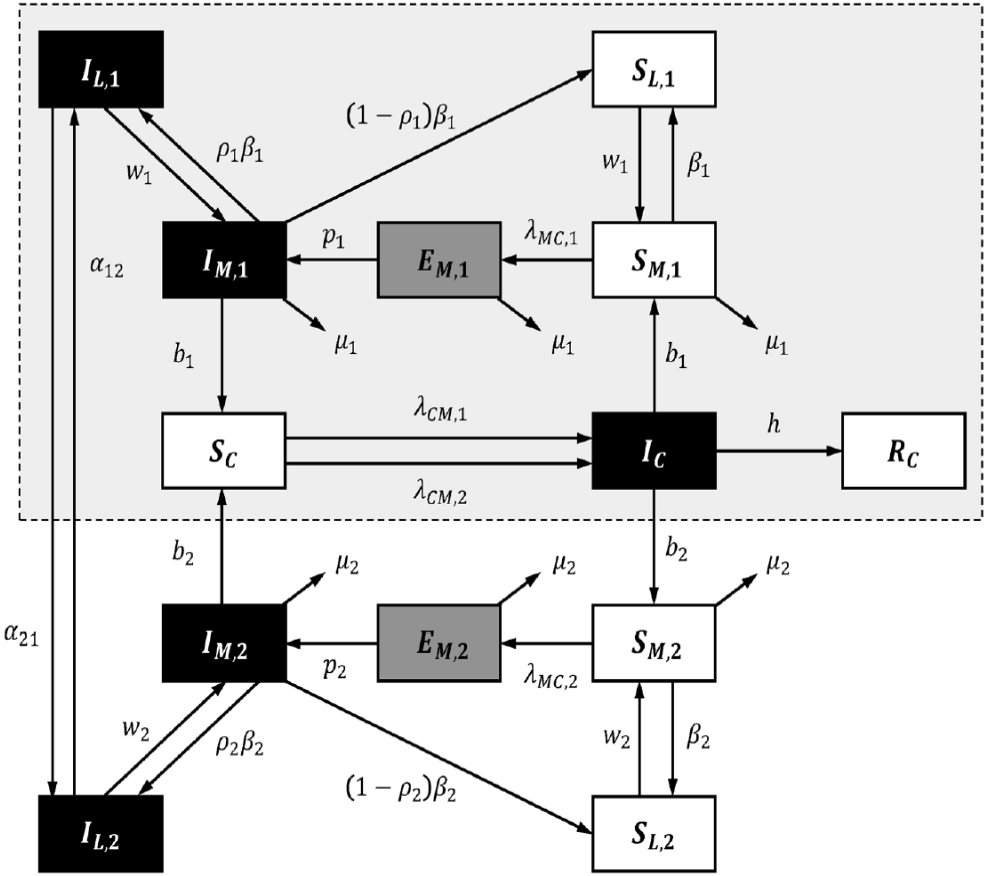
How much bed-net usage is necessary to control the spread of malaria in the community?



$$b > \frac{\beta_{max} - \mu_{v1} Q}{\beta_{max} - \beta_{min} + \mu_{max} Q} = b_c$$

With bed-net usage of 75%, R=0.4

Epidemiology of La Crosse Virus Emergence, Appalachia Region, United States

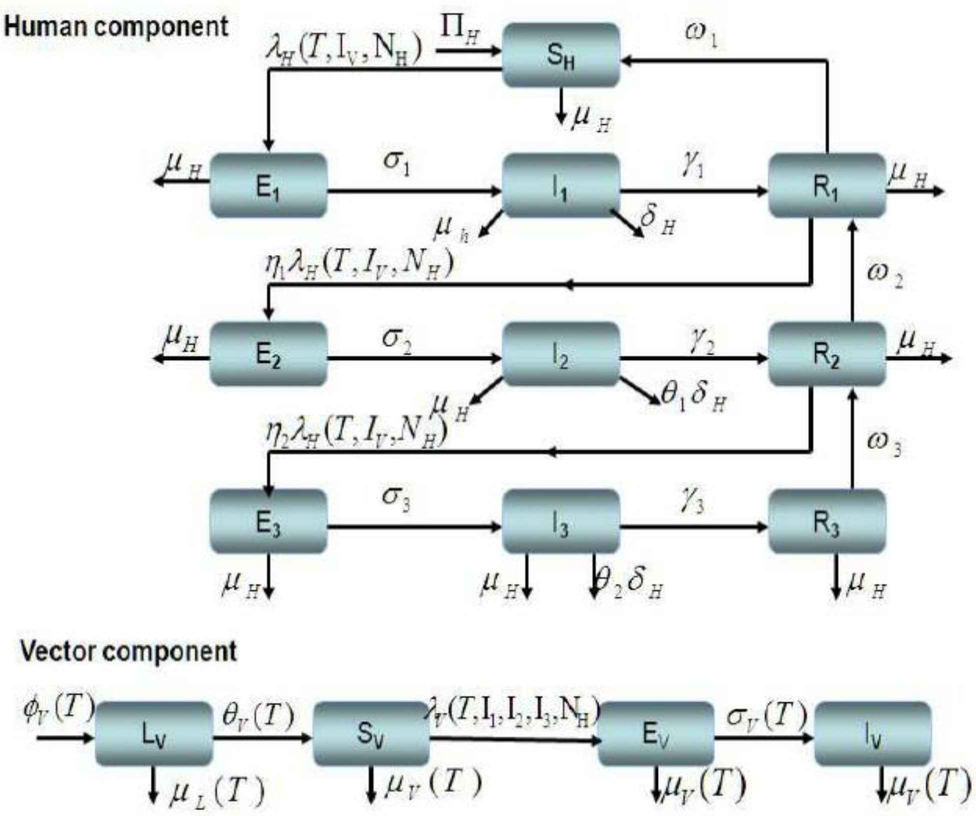


What is the role of invasive Asian tiger (*Aedes albopictus*) mosquito on the emergence of La Crosse virus (LACV)?

This model do not, however, support the hypothesis that Asian tiger mosquitoes are responsible for the recent emergence of LACV at new foci.

Bewick, S., Agusto, F., Calabrese, J. M., Muturi, E. J., & Fagan, W. F. (2016). Epidemiology of La Crosse Virus Emergence, Appalachia Region, United States. *Emerging infectious diseases*, *22*(11), 1921.

Assessing the role of temperature variations on malaria transmission dynamics



Agusto, F. B., Gumel, A. B., & Parham, P. E. (2015). Qualitative assessment of the role of temperature variations on malaria transmission dynamics. *Journal of Biological Systems*, *23*(04), 1550030.

What are the effect of temperature in sub-Saharan Africa?

Malaria-associated increases with increasing mean monthly temperature in the ranges:

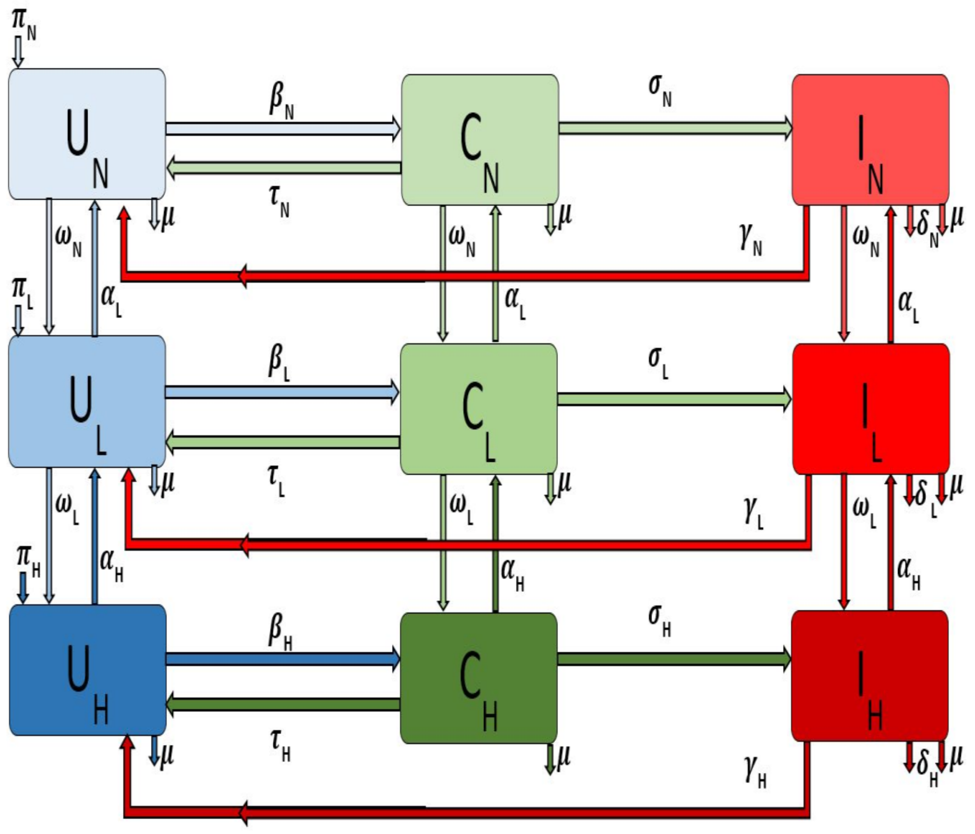
(1) $[22.6-28.6]^0C$ in the three West African cities,

(2) $[16.7-27.9]^0C$ in the three Central African cities,

(3) $[19.0-26.8]^0C$ in the three East African cities,

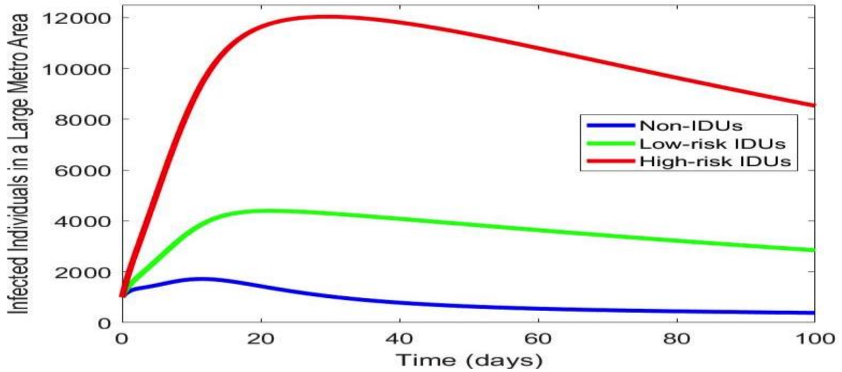
(4) $[16-25]^0C$ in Kwazulu-Natal, South Africa.

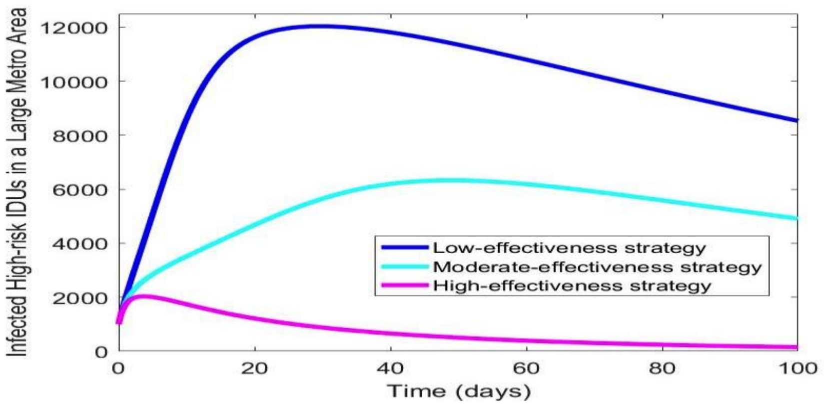
Methicillin-resistant Staphylococcus aureus among injection drug users (IDUs)



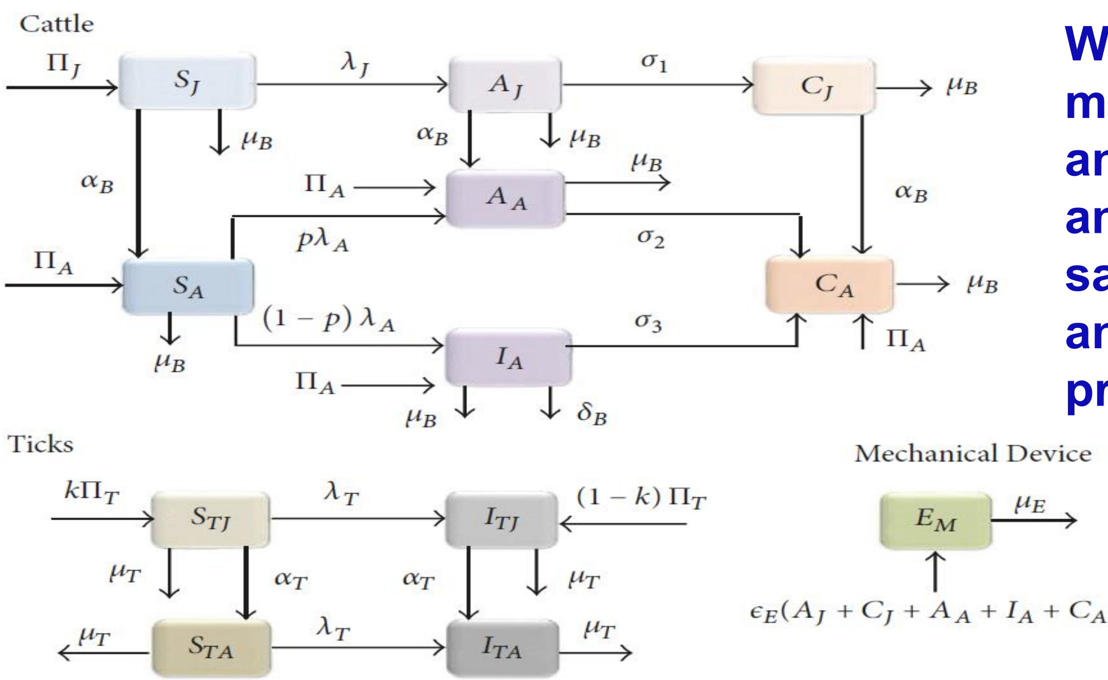
Wagner, R., & Agusto, F. B. (2018). Transmission dynamics for Methicillin-resistant Staphylococcus aureus with injection drug user. *BMC infectious diseases*, *18*(1), 69.

What is the impact of behavioral change of the IDUs on MRSA transmission in a community?





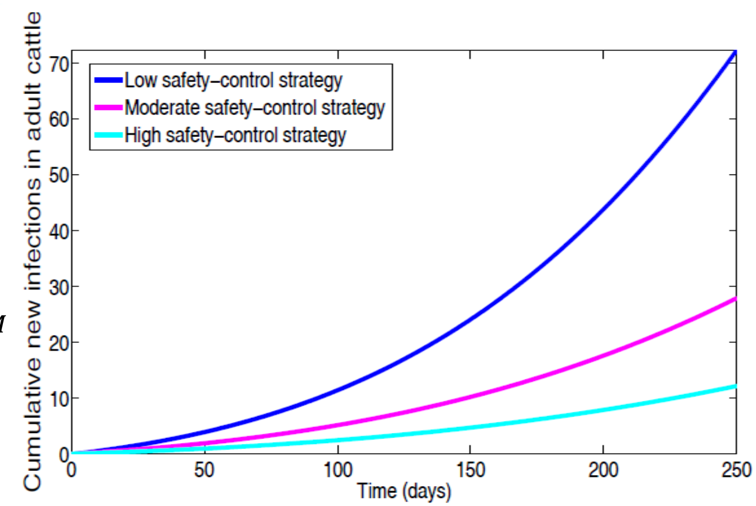
Transmission Dynamics of Bovine Anaplasmosis in a Cattle Herd



$$\lambda_J = \frac{\beta_J \phi_T (I_{TJ} + I_{TA})}{S_J + A_J + C_J} + \beta_E \phi_E E_M \quad \lambda_A = \frac{\beta_A \phi_T (I_{TJ} + I_{TA})}{S_A + A_A + C_A} + \beta_E \phi_E E_M$$

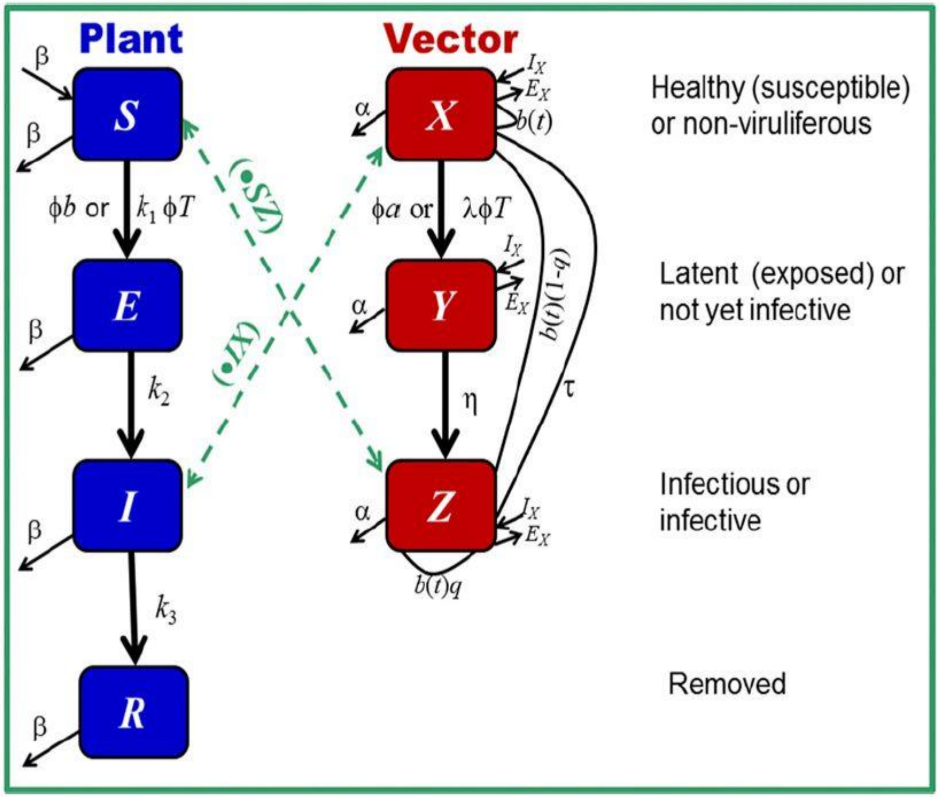
$$\lambda_T = \frac{\beta_T \phi_T (A_J + C_J + A_A + I_A)}{N_J + N_A}$$

Which control strategies is the most effective in the prevention and control of bovine anaplasmosis: bovine-culling, safety-control and, improving and maintaining good hygiene practices?

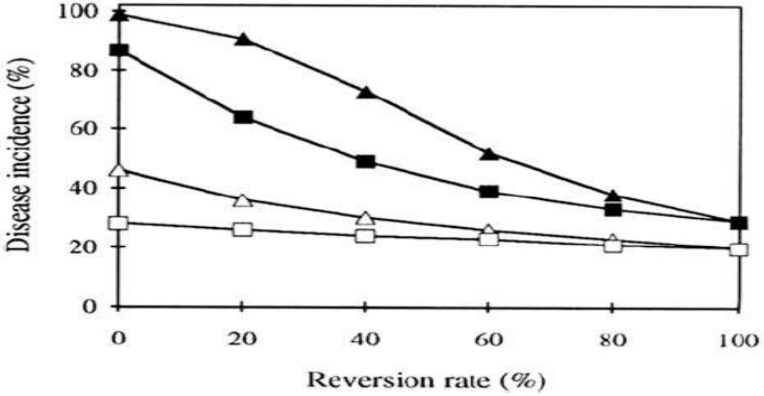


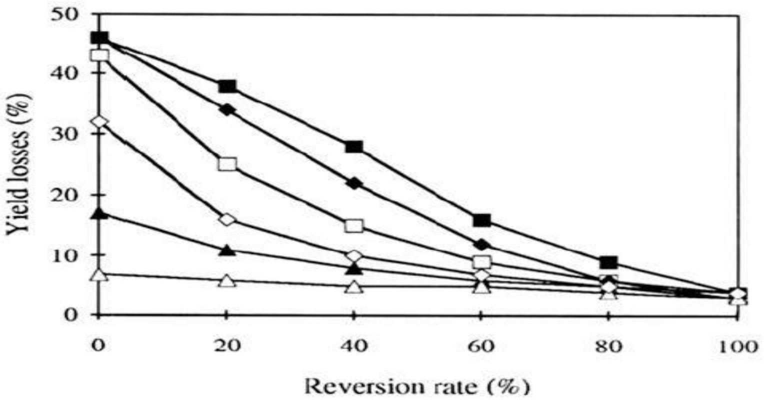
Zabel, T. A., & Agusto, F. B. (2018). Transmission Dynamics of Bovine Anaplasmosis in a Cattle Herd. *Interdisciplinary perspectives on infectious diseases*, 2018.

Plant-virus-vector interactions



What are the optimal control strategies required to minimize yield losses?





Jeger, M. J., Madden, L. V., & van den Bosch, F. (2018). Plant Virus Epidemiology: Applications and Prospects for Mathematical Modeling and Analysis to Improve Understanding and Disease Control. *Plant Disease*, *102*(5), 837-854.

Tree harvesting in age-structured forests subject to beetle infestations

What is the effect of beetle outbreaks on forest trees dynamics?

$$\frac{dB}{dt} = r_B B\left(1 - \frac{B}{K_e}\right) - \frac{\alpha B^2}{1+\beta B^2}$$

$$\frac{\partial V(a,t)}{\partial t} + \frac{\partial V(a,t)}{\partial a} = -[\mu(a) + \mu_B(a,t)]V(a,t)$$

$$0 \le t \le T, \qquad 0 \le a < A, \qquad A, T < \infty$$

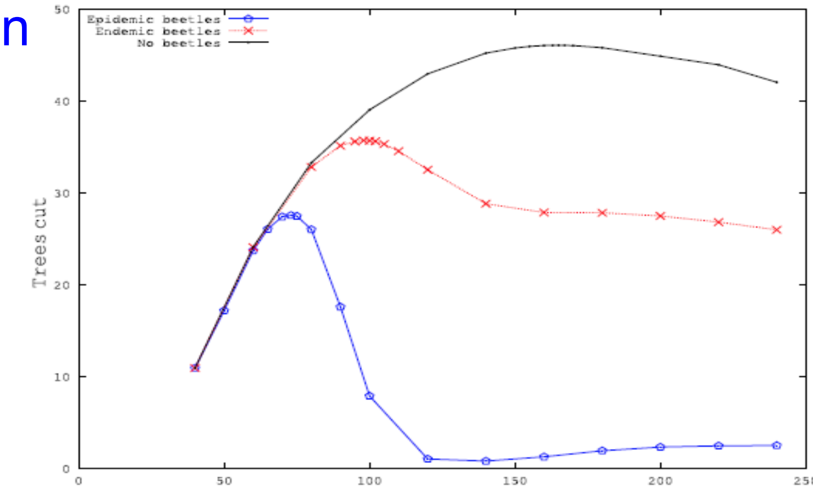
$$V(a,0) = V_0(a) \qquad V(A,0) \equiv 0$$

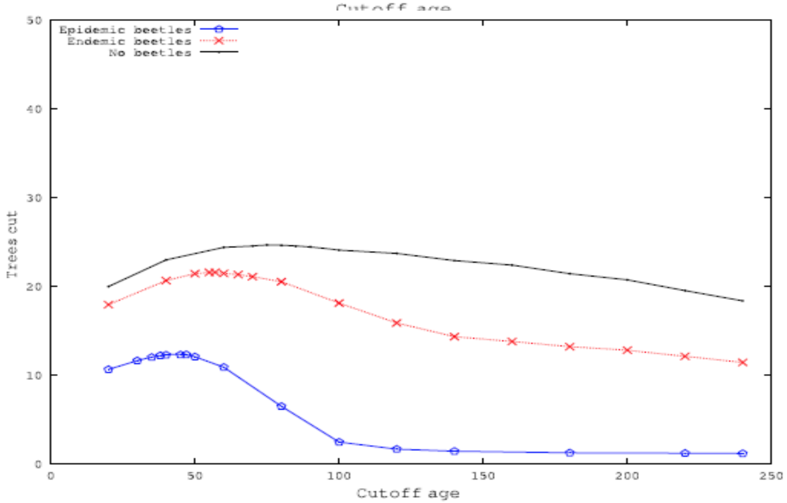
$$V(0,t) = V(t) = \int_0^A b(a)V(a,t)dt$$

What is the effect of beetle outbreaks and harvesting strategies on the harvest benefit?

$$J(u) = \int_0^T \int_0^A V(a,t)da\,\mathrm{dt}$$

Leite, M. C. A., Chen-Charpentier, B., & Agusto, F. B. (2018). A mathematical model of tree harvesting in age-structured forests subject to beetle infestations. *Computational and Applied Mathematics*, *37*(3), 3365-3384.





Optimal Control Theory

$J(u) = optimize \int_0^T f(t, x(t), u(t))dt$

subject to

$x'(t) \ = \ g(t, x(t), u(t))$

$x(0) \ = \ x_0$ and $x(T)$ free

What is the optimal piecewise continuous control $u^*(t)$ and the $x^*(t)$ associated state variable that optimizes the objective functional $J(u)$?

Pseudo-algorithm

- Optimal Control $u^*(t)$ achieves the optimum
- Put $u^*(t)$ into state equation and obtain $x^*(t)$
- $x^*(t)$ corresponding optimal state
- $u^*(t), x^*(t)$ optimal pair

Lenhart, S., & Workman, J. T. (2007). *Optimal control applied to biological models*. Crc Press.

Maximizing tree harvesting benefit from forests under insect infestation disturbances

$$\frac{dB(a,t)}{dt} = r_b B(a,t)\left(1 - \frac{B(a,t)}{K_e(a)}\right) - \frac{\alpha B(a,t)^2}{1+\beta B(a,t)^2}$$

$$\frac{\partial V(a,t)}{\partial t} + \frac{\partial V(a,t)}{\partial a} = -[\mu(a,t) + \mu_B(a,t) + u(a,t)]V(a,t)$$

$$\mu_B(a,t) = f_k(a)B(a,t)$$

$$0 \le t \le T, 0 \le a < A, A, T < \infty$$

$$V(a,0) = V_0(a) \quad V(A,0) \equiv 0$$

$$V(0,t) = \int_0^A b(a)V(a,t)da$$

$$B_T(0,t) = \int_0^A B(a,t)V(a,t)da$$

1. Total number of trees harvested

$$J_1(u) = \int_0^T \int_0^A \omega_1 u(a,t)V(a,t)da\, \mathrm{dt}$$

2. Total amount of wood harvested including trees killed by beetles and other natural causes

$$J_2(u) = \int_0^T \int_0^A \begin{matrix}[\omega_1 u(a,t) + \omega_2(\mu_B(a,t) \\ + \mu(a,t))]V(a,t)da\end{matrix}\ \mathrm{dt}$$

3. Total benefit

$$J_3(u) = \int_0^T \int_0^A \begin{matrix}[\omega_1 u(a,t) + \omega_2(\mu_B(a,t) \\ + \mu(a,t))]V(a,t)da\end{matrix}\ \mathrm{dt}$$

$$-\int_0^T \int_0^T \omega_3 u^2\,(a,t)da\ dt$$

Leite, M. C., Chen-Charpentier, B., & Agusto, F. B. (2018). Maximizing tree harvesting benefit from forests under insect infestation disturbances. *PloS one*, *13*(8), e0200575.

Optimal harvesting strategies for timber and non-timber forest products (NTFPs) in tropical ecosystem

$$\frac{dx(t)}{dt} = r(t)x(t)\left(1 - \frac{x(t)}{K}\right) - h_L(t)x(t)$$

$$\tau\frac{dr(t)}{dt} = r_e - r(t) - [\alpha \mathrm{h}_N(t) + \beta \mathrm{h}_L(t)]$$

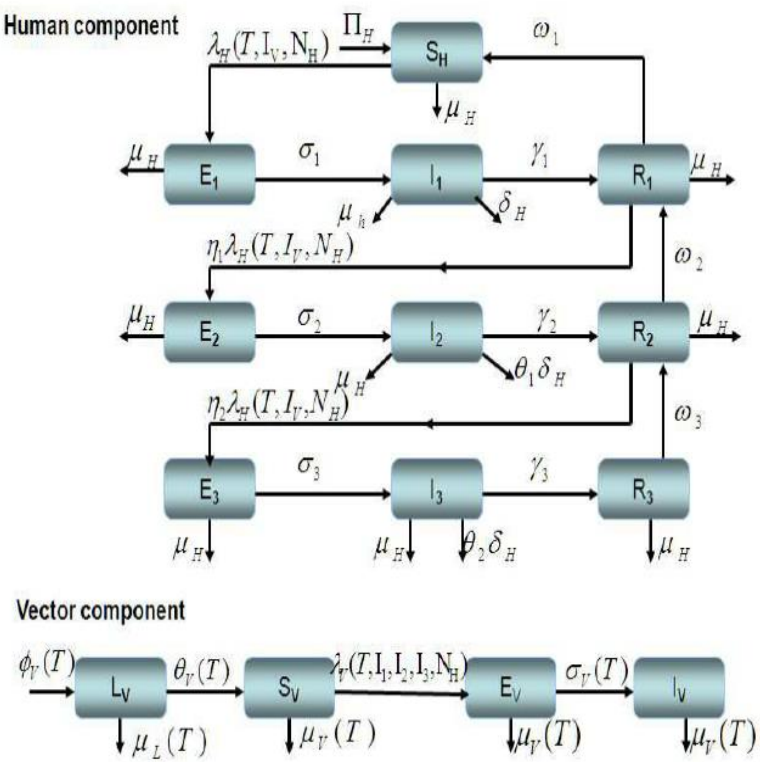
$$x(0) = x_0,\ r(0) = r\_e$$

$$J(h_L, h_N) = A_T\, x(T) + \int_0^T \mathrm{e}^{-\delta\, t}[Ax(t) + B_1 h_L(t)$$

$$+B_2 h_N(t)x(t) - C_1 h_L^2(t) - C_2 h_N^2(t)]dt$$

Gaoue, O. G., Jiang, J., Ding, W., Agusto, F. B., & Lenhart, S. (2016). Optimal harvesting strategies for timber and non-timber forest products in tropical ecosystems. *Theoretical ecology*, *9*(3), 287-297.

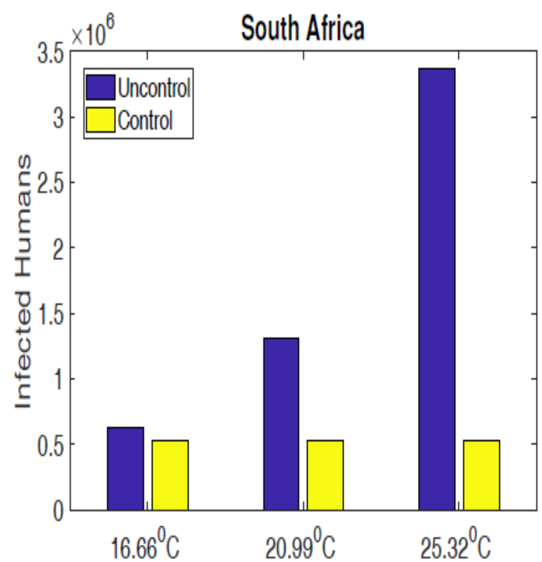
Optimal control & temperature variations of malaria transmission dynamics

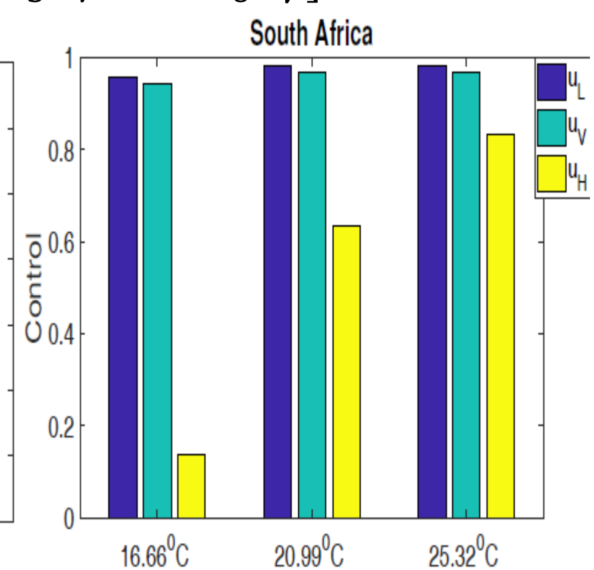


F.B. Agusto (2018)
Optimal Control and Temperature Variations of Malaria Transmission Dynamics. Submitted to Mathematical Biosciences

What are the optimal control strategies under changing temperatures in sub-Saharan Africa?

$$J(u_H, u_L, u_V) = \int_0^T [A_1 I_H + B_1 L_V + B_2 S_V + B_3 E_V + B_4 I_V + C_1 u_H + \epsilon C_2 u_H^2 + C_3 u_L + \epsilon C_4 u_L^2 + C_5 u_V + \epsilon C_6 u_V^2]$$





MATHEMATICAL FRONTIERS

Mathematics of Epidemics

Calistus Ngonghala,
University of Florida, Gainesville

Assistant Professor
Mathematical Biology
University of Florida, Gainesville

Understanding extreme poverty from an epidemiological-economic perspective

Background and empirical trends

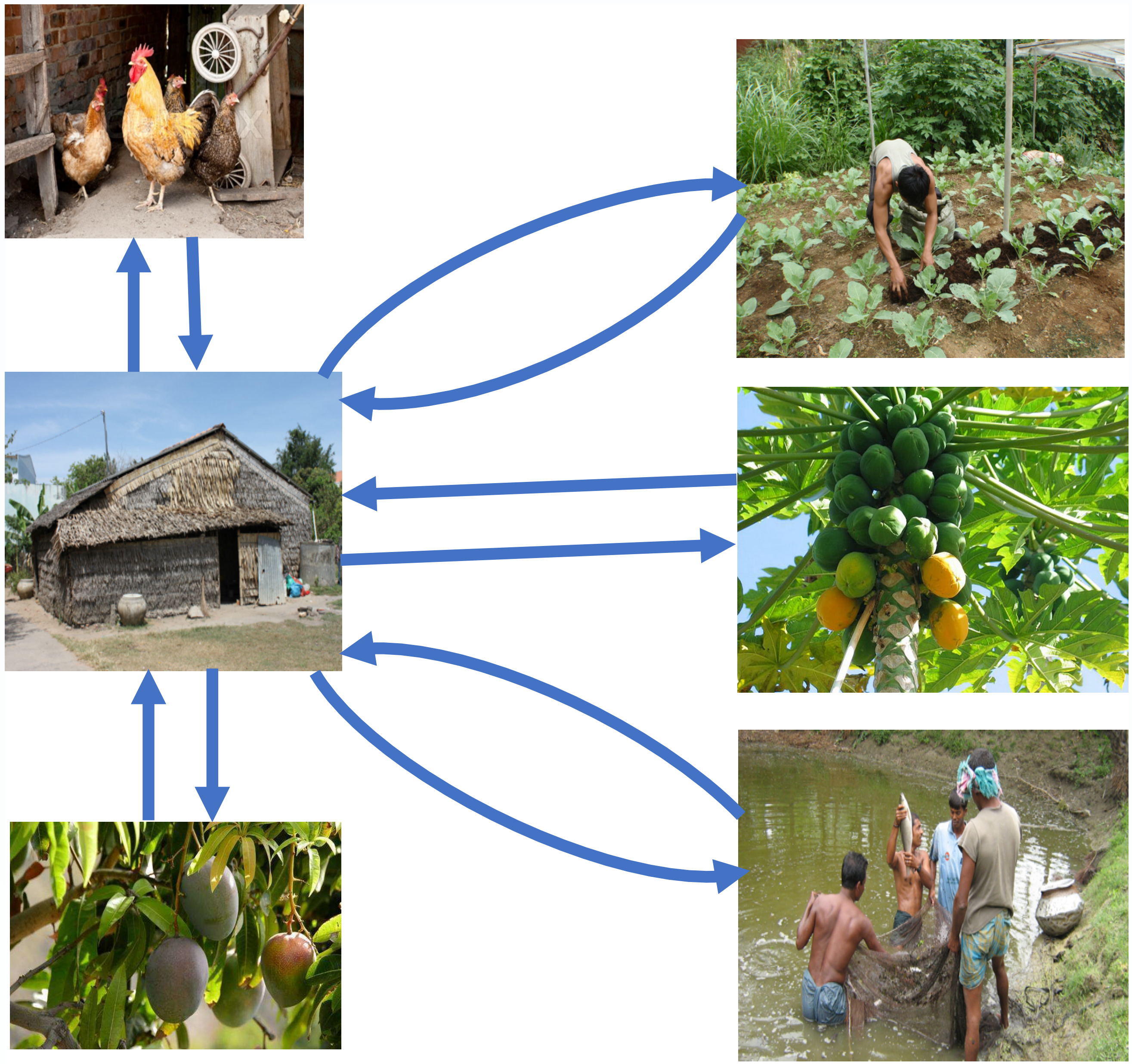
- About 1.94 billion people lived in extreme poverty in 1981
- Currently, about 746 million people live in extreme poverty
- $\approx 61\%$ decline in number of poor
- Reduction more significant in middle-income countries
- 33% of the extreme poor live in low-income countries, compared to 13% in 1981
- No significant change for the poor in low-income countries

Background

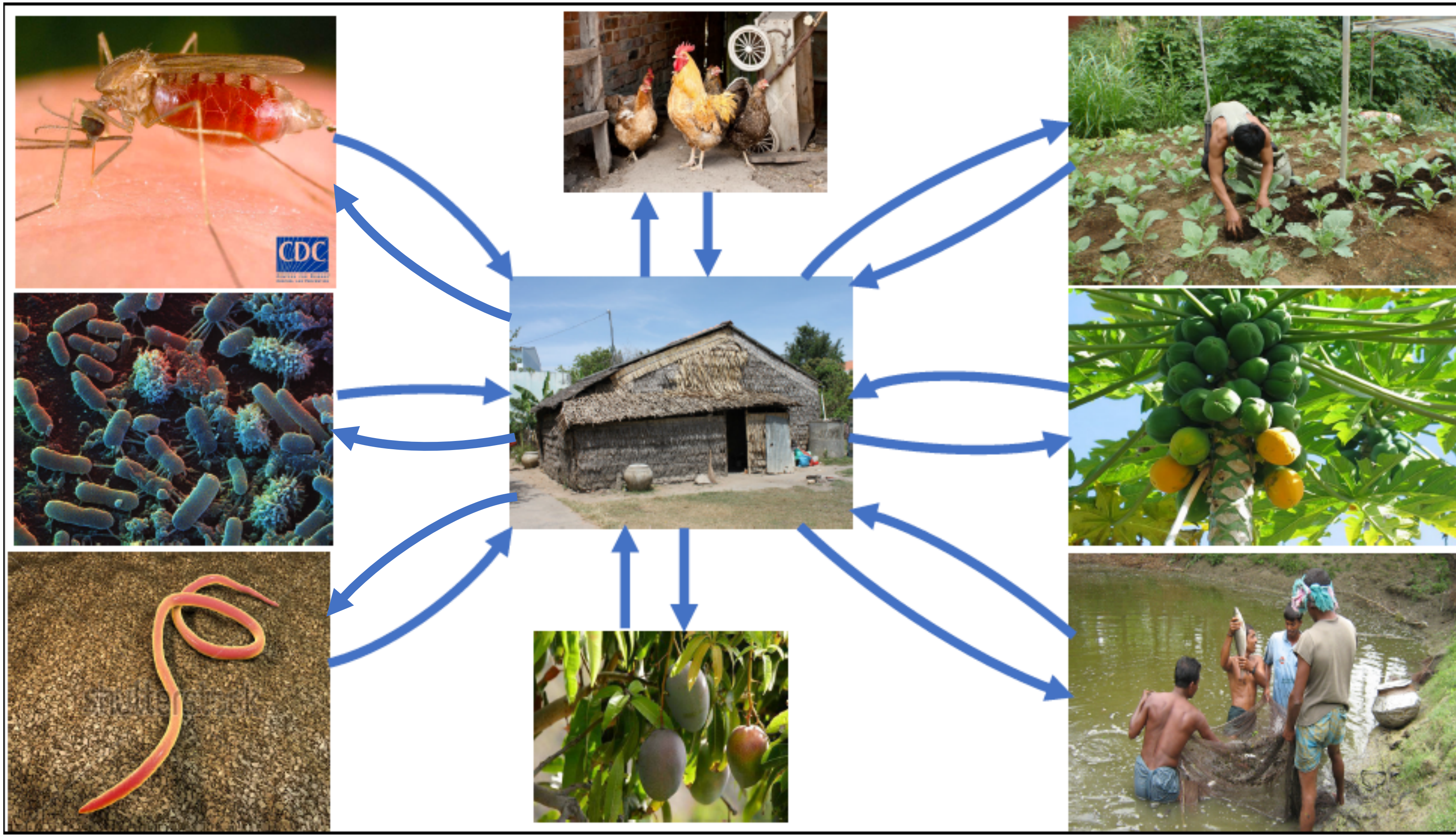
- 70% of the global poor live in rural areas, mostly subsistence
- 35% suffer from chronic malnutrition
- 75% of deaths among the poor are due to infectious diseases

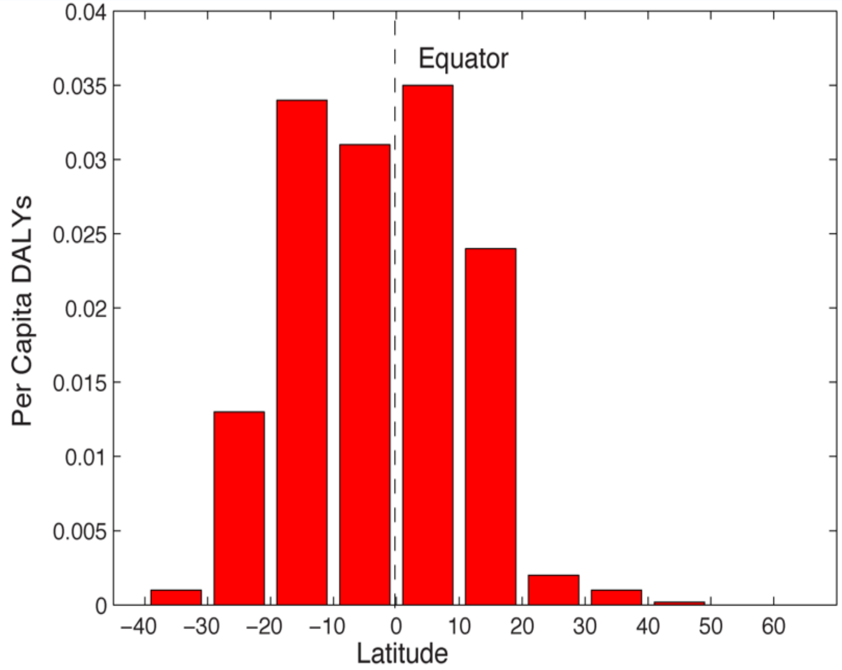
Major characteristics of the rural poor

Subsistence life styles and high disease burden

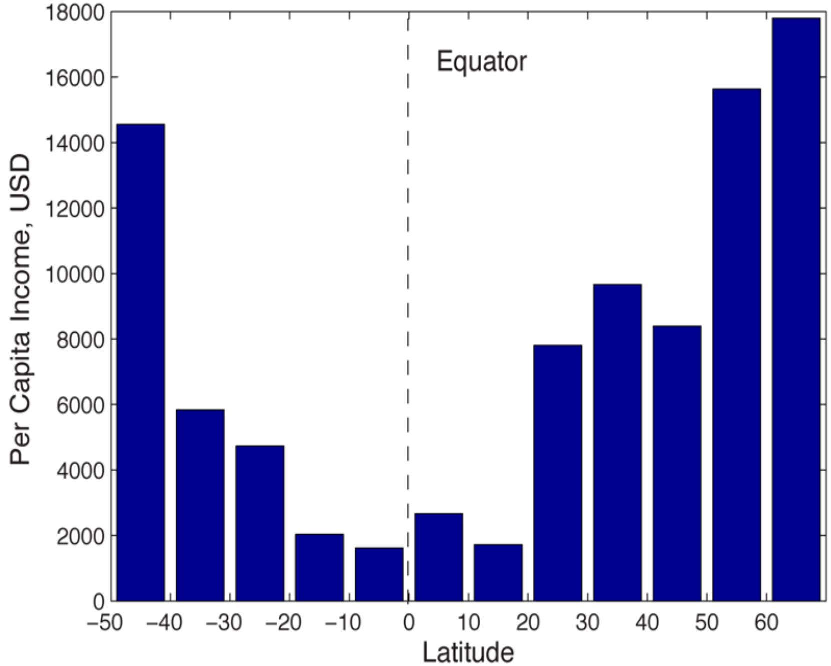


Subsistence life styles and high disease burden





Vector-borne and parasitic disease burden

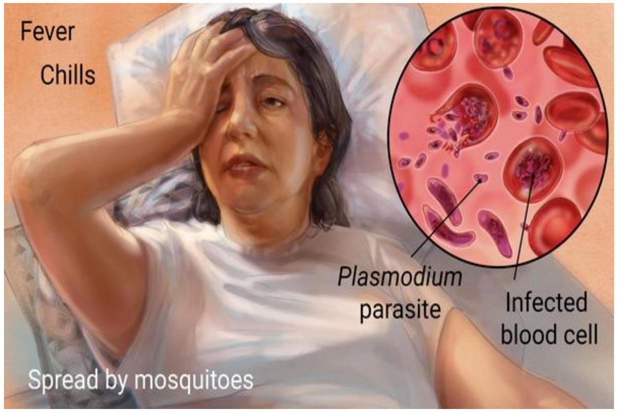


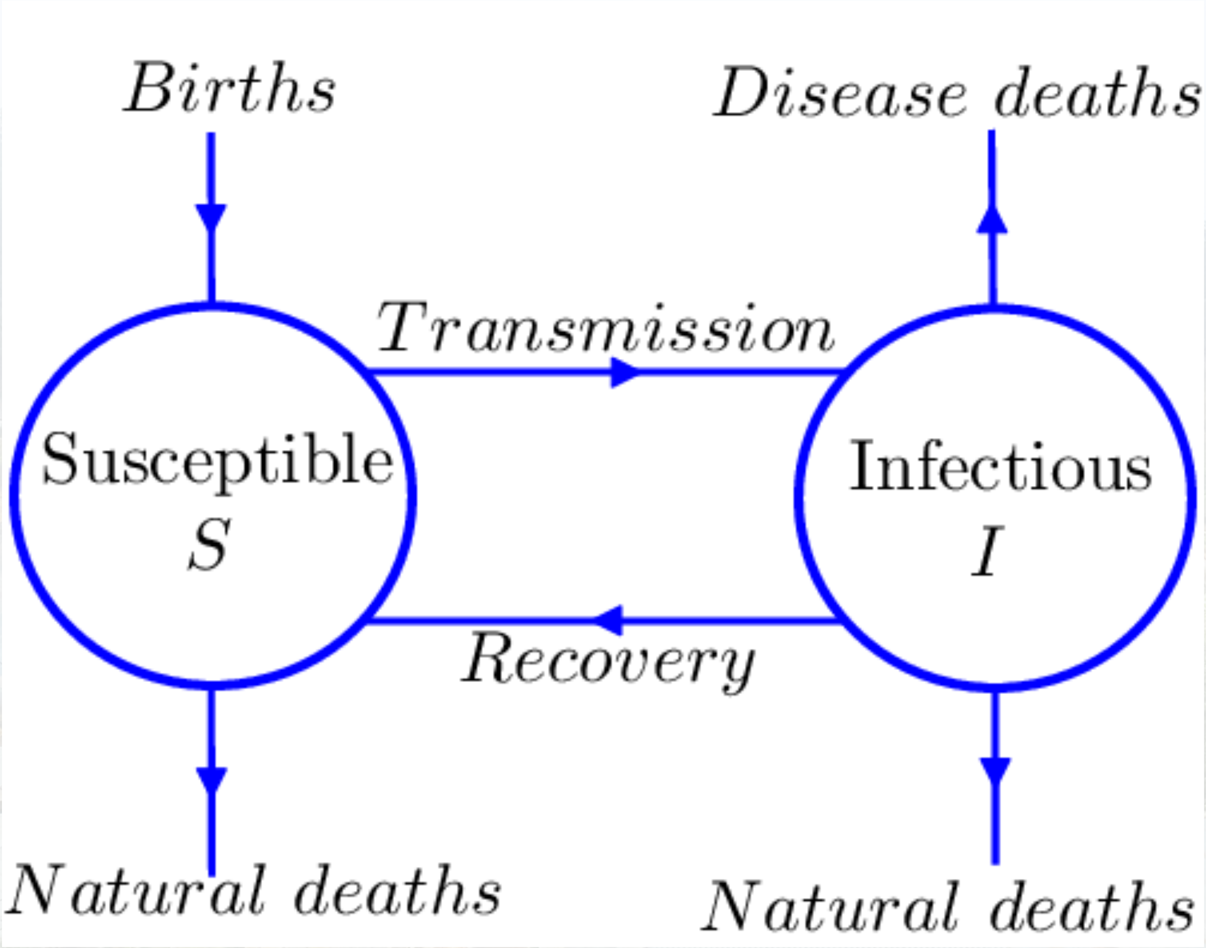
Income

Bonds et al. (2012) PLoS Biology (https://doi.org/10.1371/journal.pbio.1001456)

Association between poverty and disease

- Malaria reduced per capita income by 1.3% (Gallup and Sachs, 2001)
- Hookworm reduced income by 35% (Bleakly, 2008)
- Nutrition supplements increased wages by 47% (Hoddinot et al., 2008)
- Deworming reduced absenteeism by 25% and improved exam. scores (Miguel and Kremer, 2003)

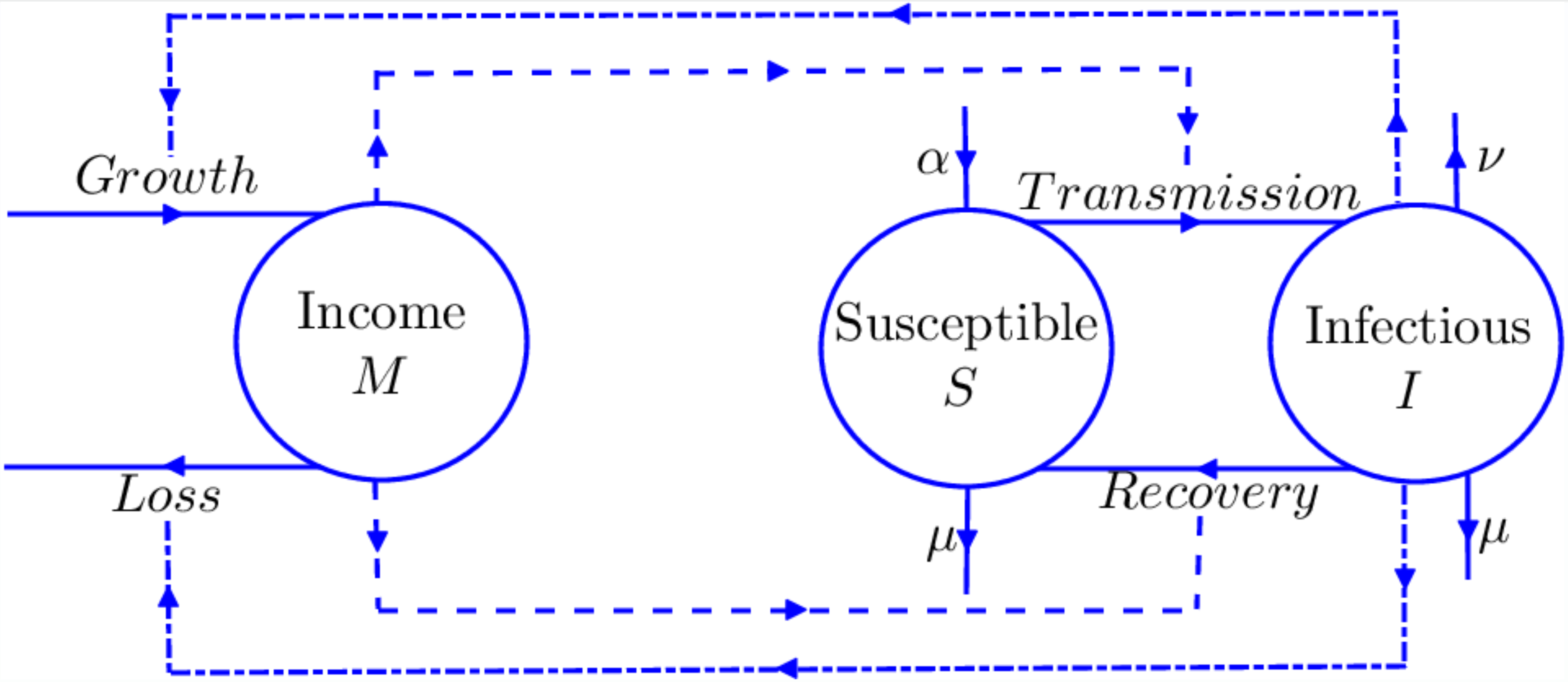


Disease model

$$\dot{I} = \beta(1 - I)I - (\alpha + \gamma + \nu)I + \nu I^2.$$

Coupled disease-economic system

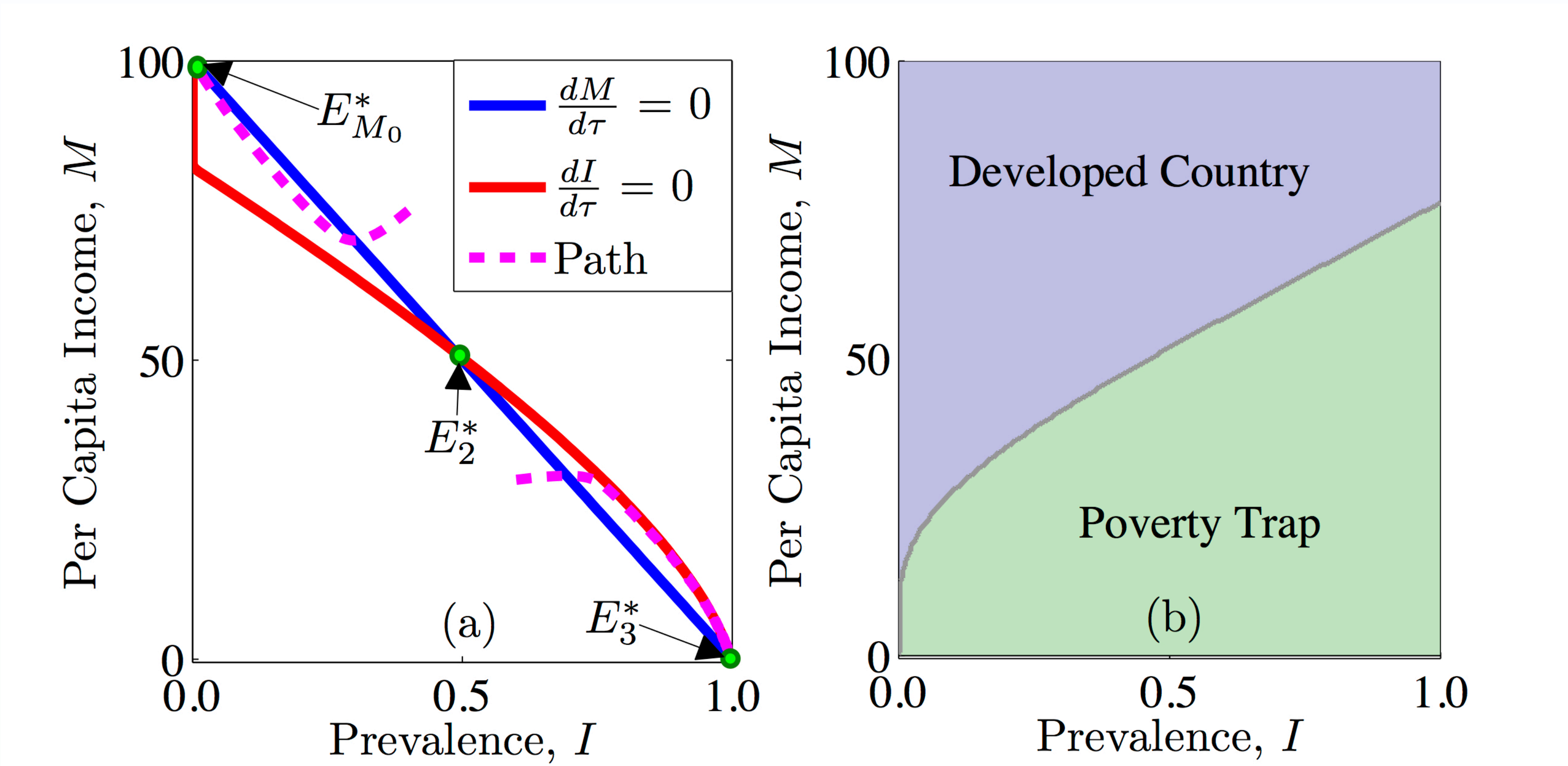


Basis of feedback between disease and income

- Disease transmission and recovery depend on income
- Income, M, depends on disease prevalence, I.

$$\begin{aligned} \dot{I} &= \beta(M)(1-I)I - (\alpha + \gamma(M) + \nu)I + \nu I^2, \\ \dot{M} &= -rM(M - M_0(1-I)). \end{aligned}$$

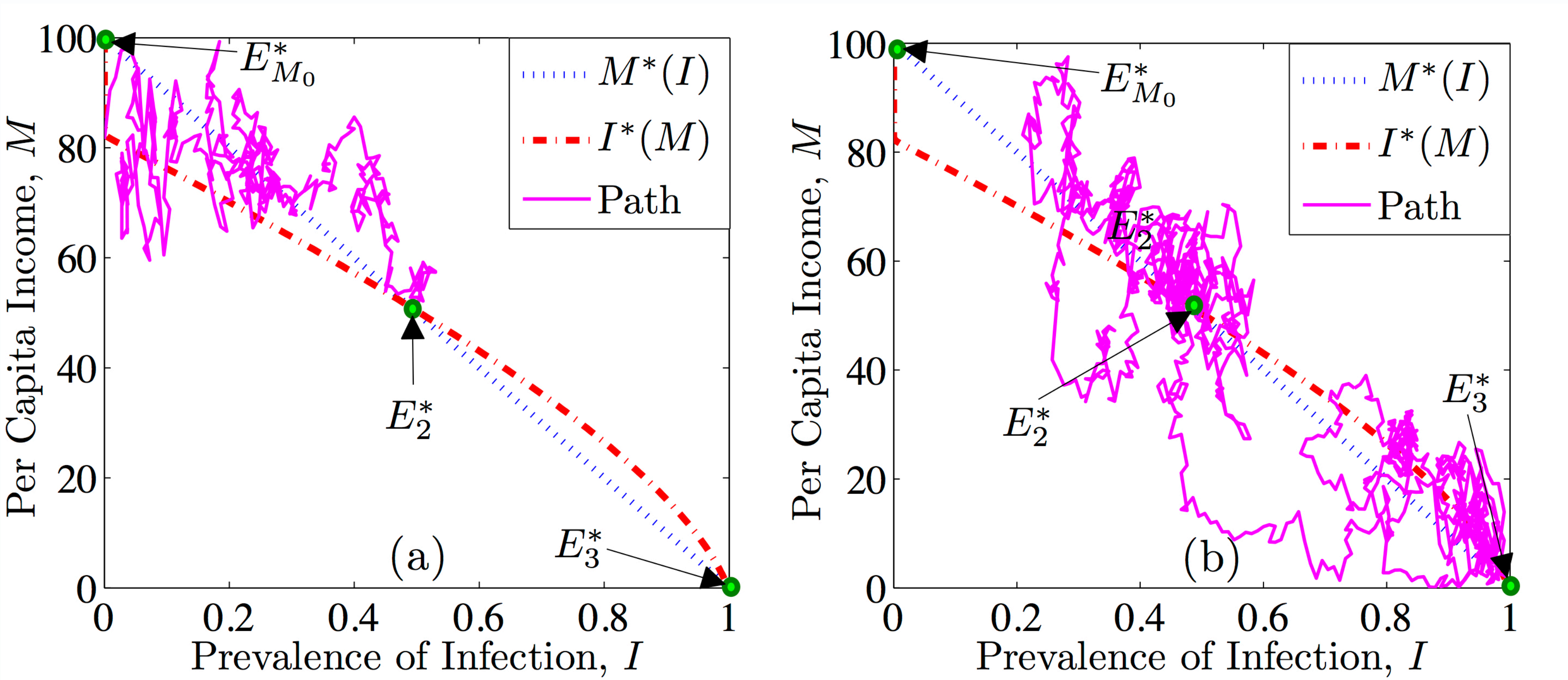
Dynamics of deterministic system



- Population is stuck in poverty trap or enjoys development
- Breaking trap requires substantial health and economic efforts

Plucinski MM, Ngonghala CN, Bonds M (2011) Journal of The Royal Society Interface

Stochastic model: Path to development or poverty trap



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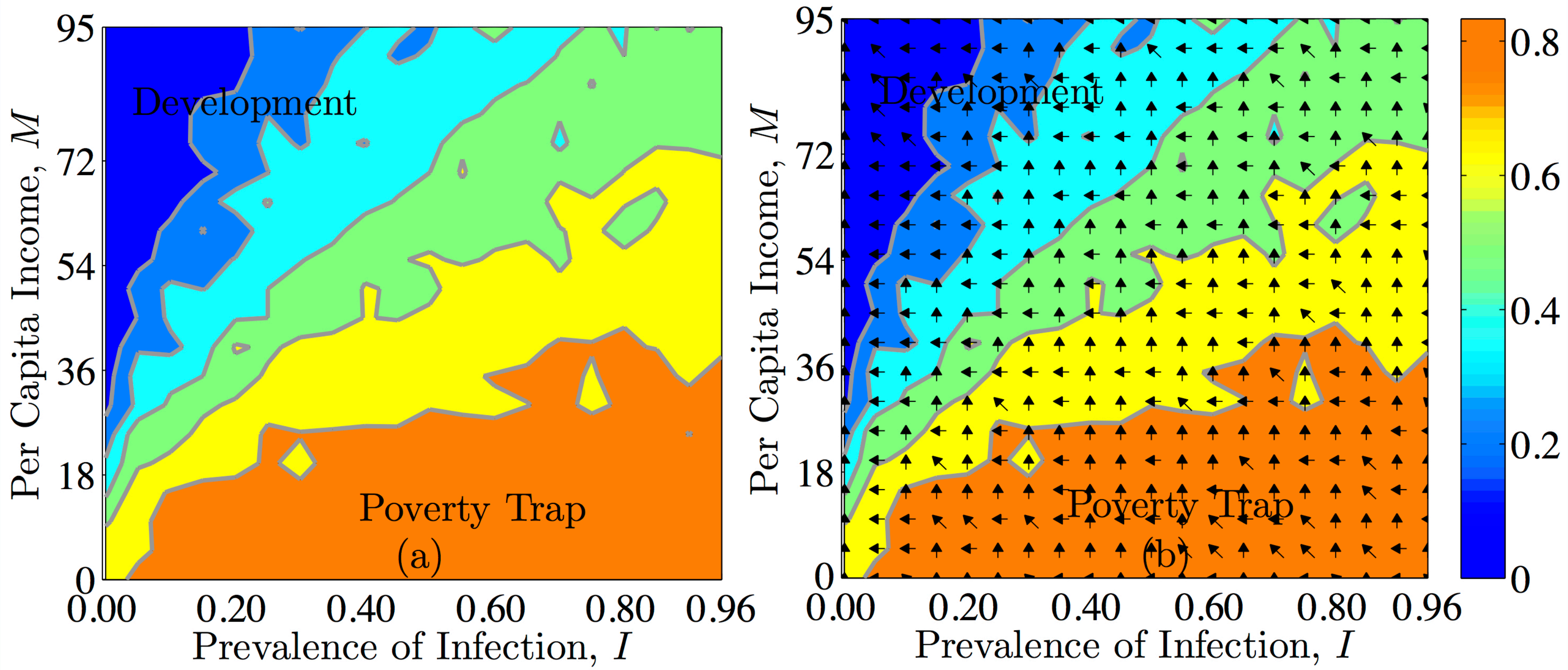
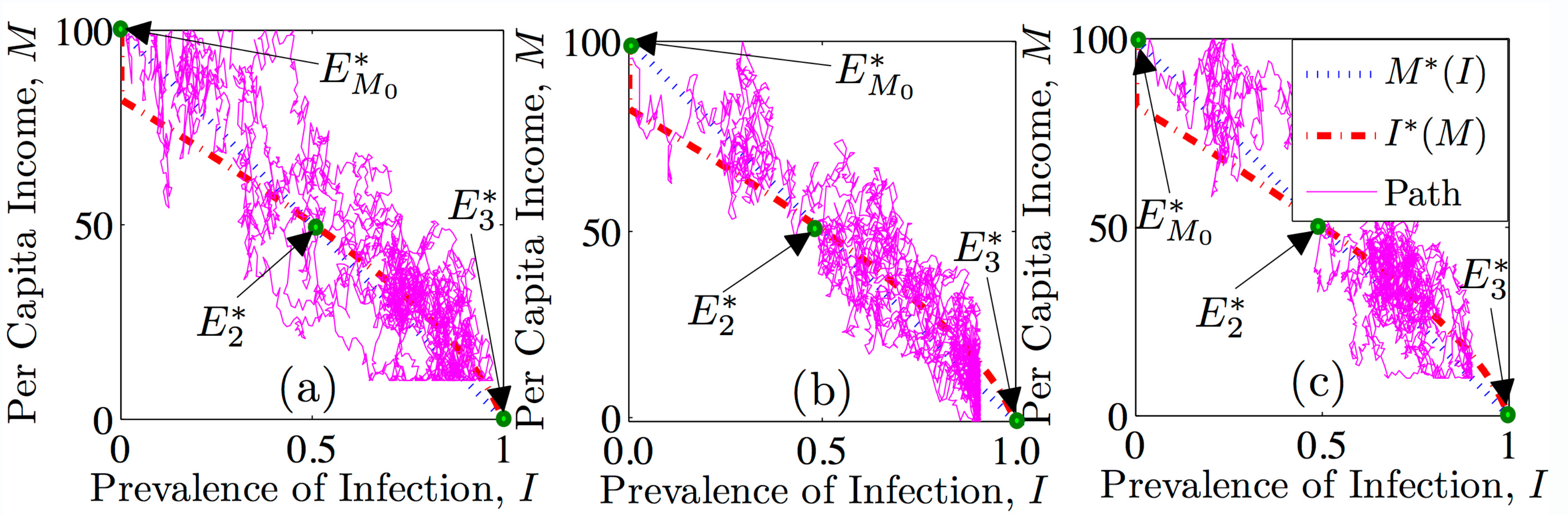


- Best strategy depends on status of income and disease
  - Increase income when arrow points vertically upward
  - More health when arrow points horizontally to the left
  - Both health and income when arrow points diagonally upwards

Plucinski MM, Ngonghala CN, Bonds MH (2011) *Journal of The Royal Society Interface*

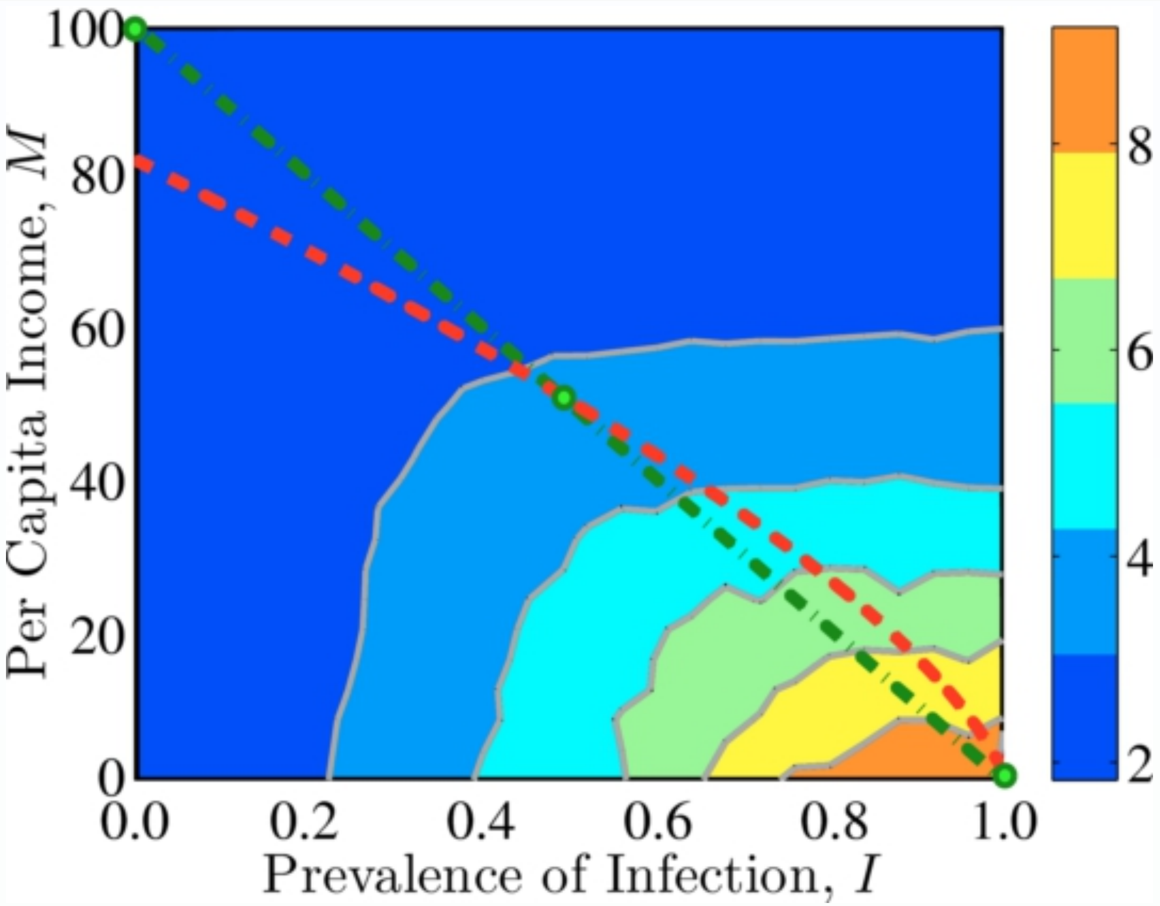
Safety nets



- Single safety nets can lead to development
- Double safety net leads to shorter time to development

Plucinski MM, Ngonghala CN, Bonds MH (2011) *Journal of The Royal Society Interface*

Rate of development

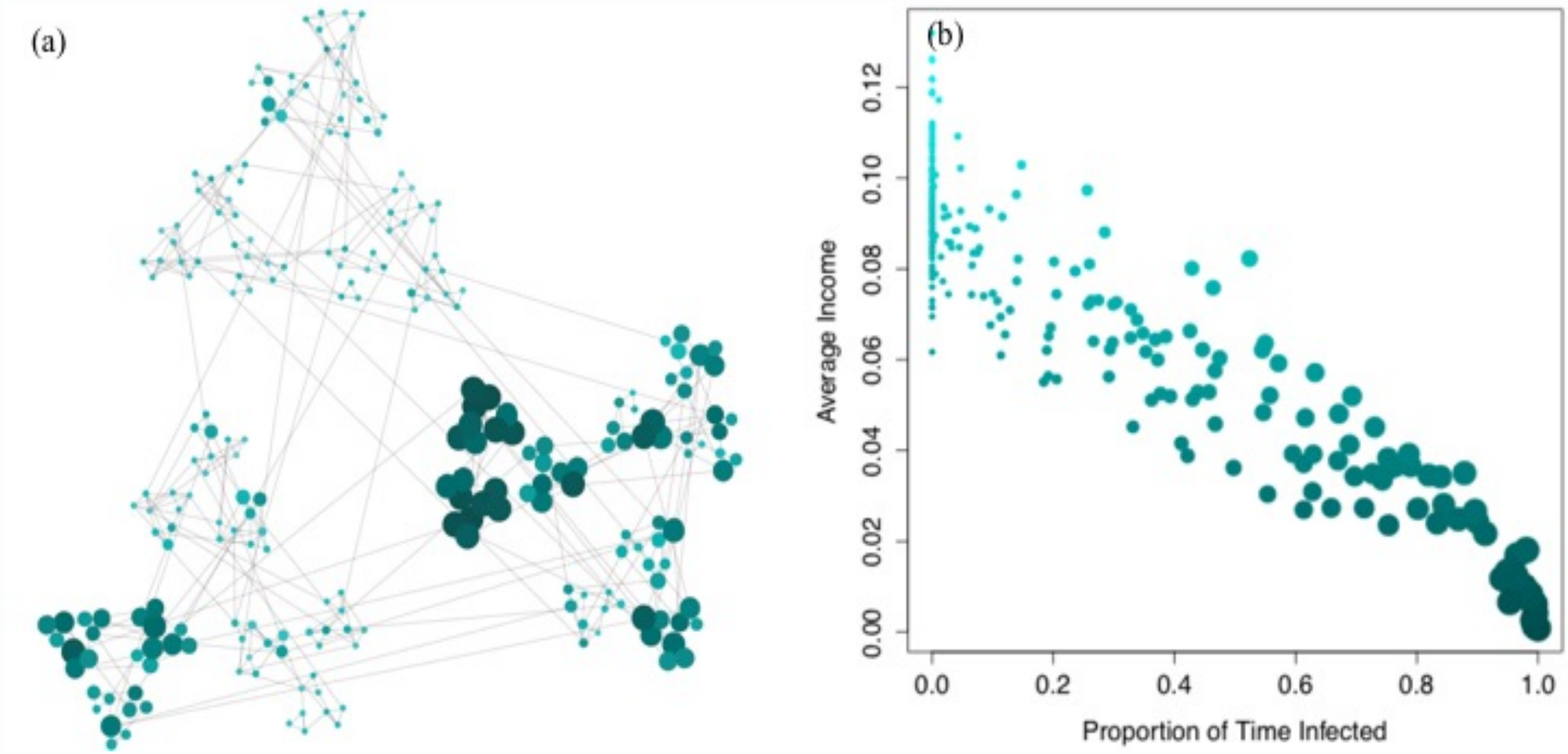


Average time to attain the development equilibrium from initial conditions reinforced by safety nets.

- Location of safety net determines rate of development

Plucinski MM, Ngonghala CN, Bonds MH (2011) *Journal of The Royal Society Interface*

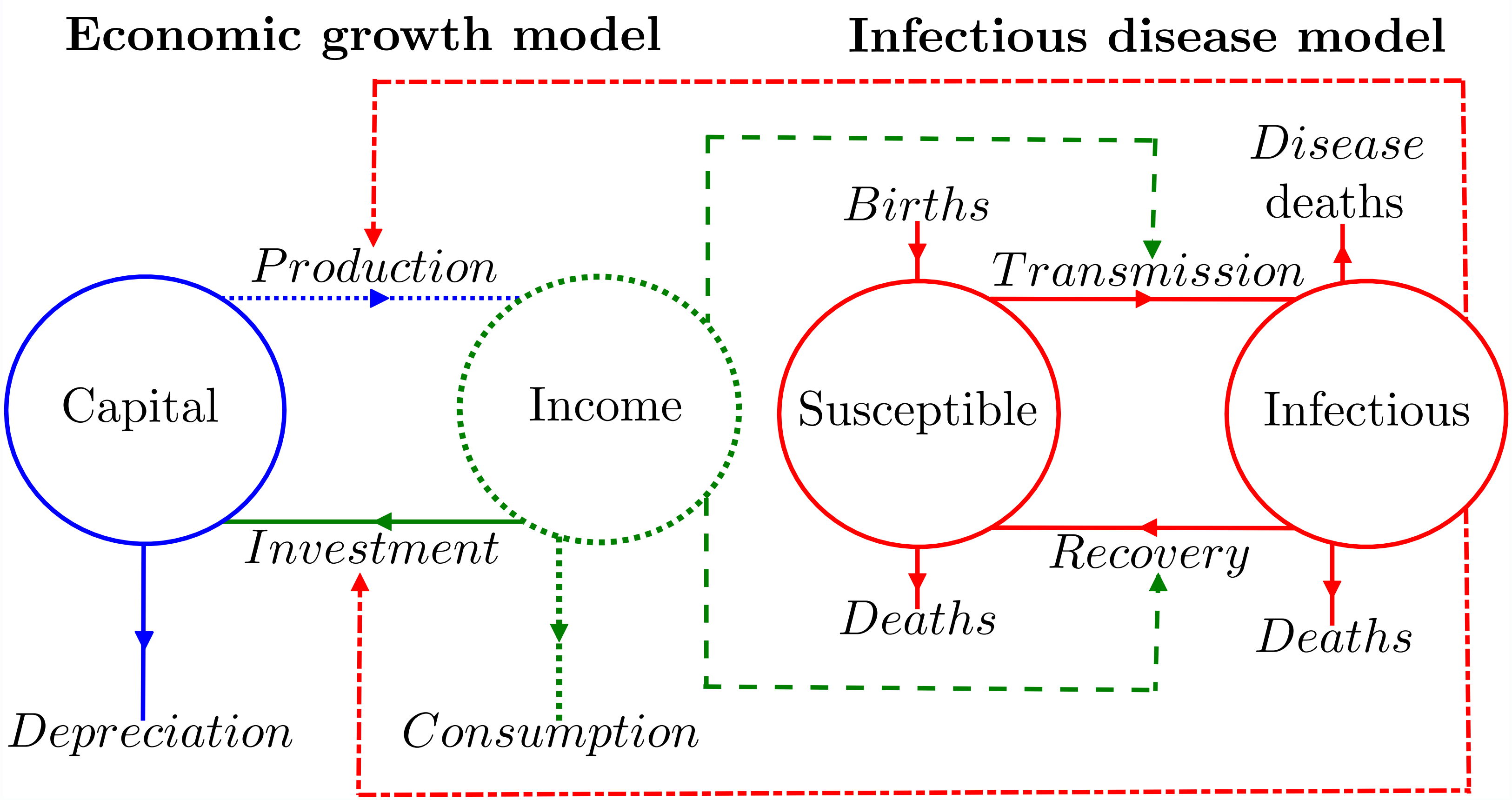
Within population poverty traps



a)-b) Each point is an individual. Darker points: lower income, larger points: greater time spent infected. a) Equilibrium distribution of health and income in the network. b) Average long-term income versus proportion of time spent infected.

Plucinski et al. (2013) *Journal of The Royal Society Interface*

Economic growth theory



$$\dot{I} = \beta(y)(1 - I)I - (\alpha + \gamma(y) + \nu)I + \nu I^2,$$

General model

- Two broad classes of state variables
  - capital – economic or biological
  - natural enemies of capital

$$Rate\ of\ change = Growth - Loss$$

$$\begin{aligned} \dot{x}_i &= \psi_i(\mathbf{x}, \mathbf{z}, f(\mathbf{x}, \mathbf{z})) - \Delta_i(\mathbf{x}, \mathbf{z}, f(\mathbf{x}, \mathbf{z})), \quad (1) \\ \dot{z}_j &= \beta_j(\mathbf{x}, \mathbf{z}, f(\mathbf{x}, \mathbf{z})) - \Gamma_j(\mathbf{x}, \mathbf{z}, f(\mathbf{x}, \mathbf{z})). \quad (2) \end{aligned}$$

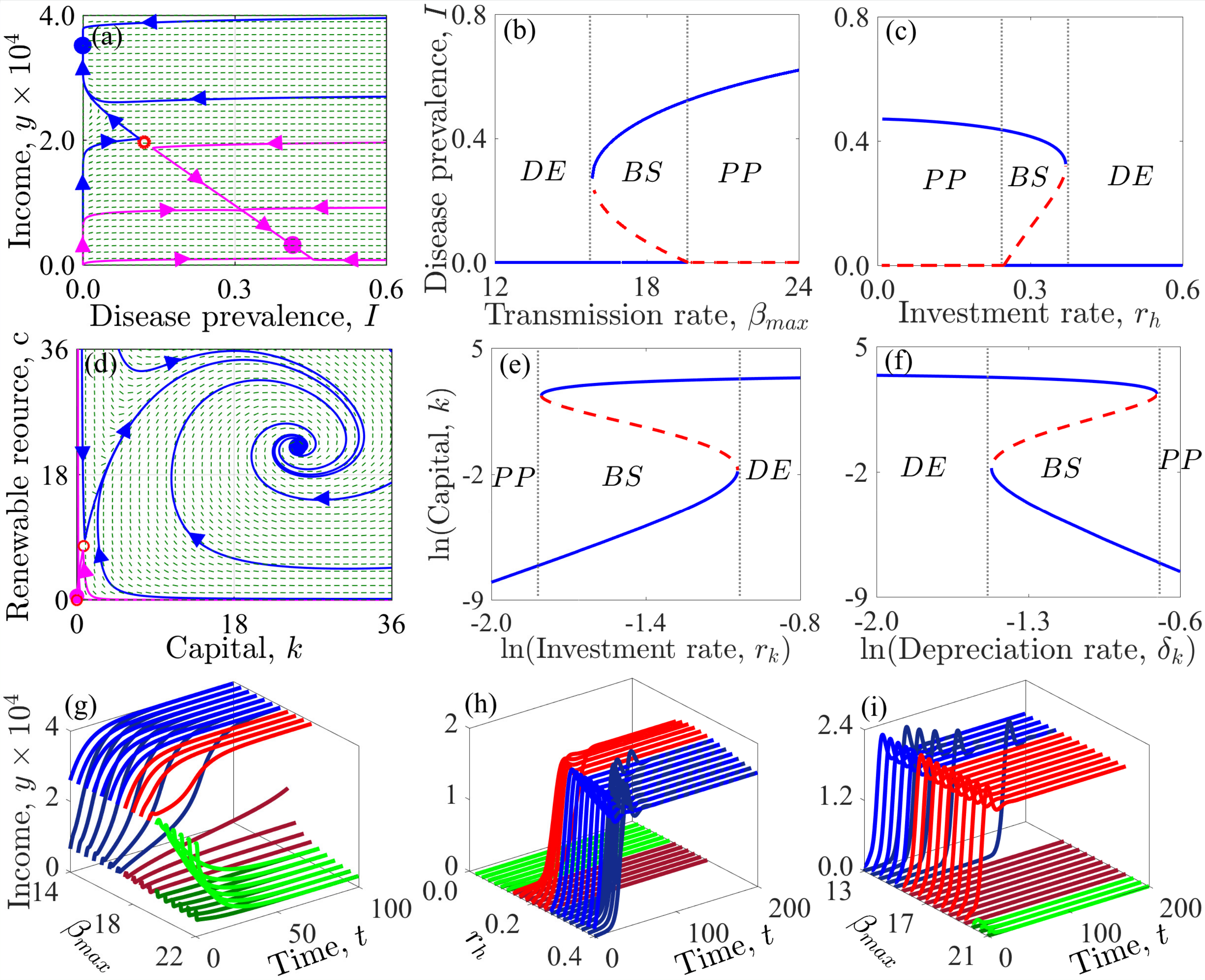
Examples of capital

- Physical capital
- Human capital
- Renewable resource
- Land-use change

Examples of natural enemies

- Infectious diseases of humans
- Diseases of animals
- Plant diseases

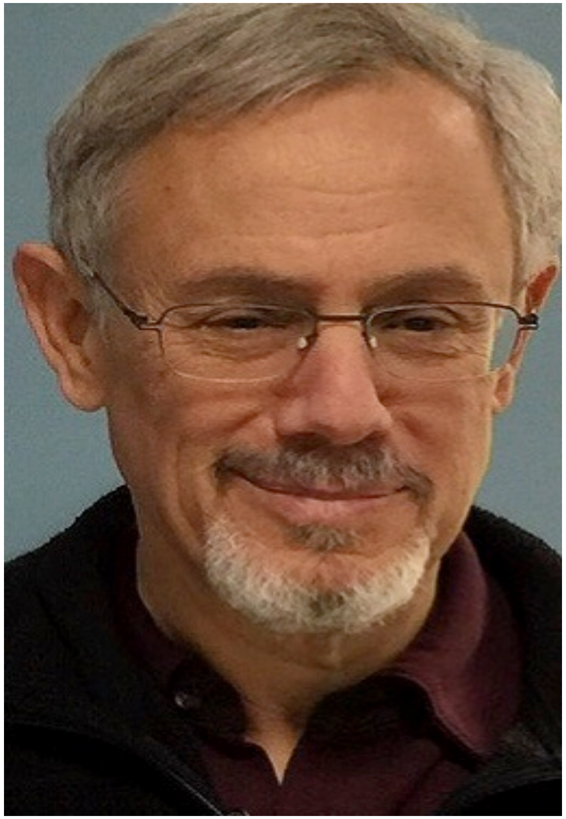
Results



(a)
Income, $y \times 10^4$
Disease prevalence, I
(b)
Disease prevalence, I
DE
BS
PP
Transmission rate, β_{max}
(c)
PP
BS
DE
Investment rate, r_h
(d)
Renewable reource, c
Capital, k
(e)
ln(Capital, k)
PP
BS
DE
ln(Investment rate, r_k)
(f)
DE
BS
PP
ln(Depreciation rate, δ_k)
(g)
Income, $y \times 10^4$
β_{max}
Time, t
(h)
r_h
Time, t
(i)
β_{max}
Time, t

MATHEMATICAL FRONTIERS

Mathematics of Epidemics



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July 9: *Cryptography and Cybersecurity*

August 13: *Machine Learning for Genomics and Medicine*

September 10: *Logic and Foundations*

October 8: *Quantum Physics and String Theory*

November 12: *Quantum Encryption*

December 10: *Machine Learning and Text*

*** *Recording posted***

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