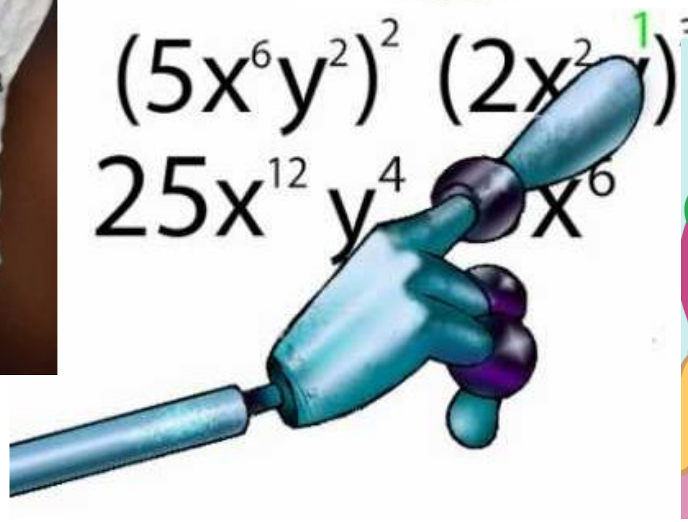
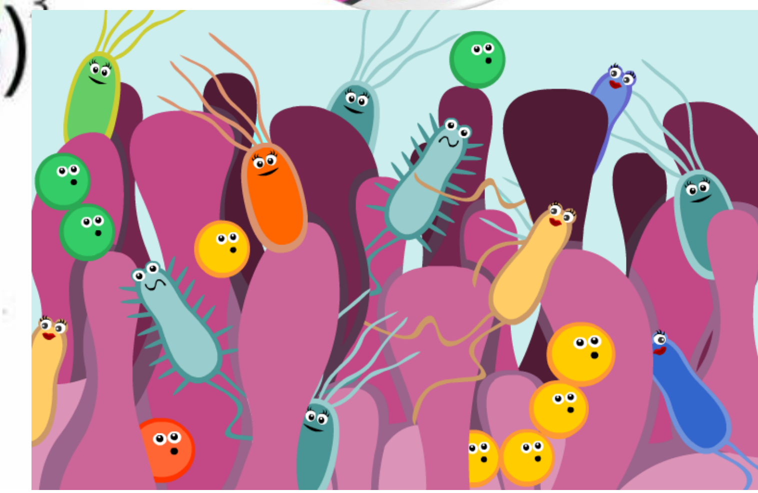
Fighting Diseases with Math





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Popular Science Talks, Science Outreach Programme, NCL Innovation Park, October 19, 2014


HOW DO SOME PEOPLE MANAGE TO UNDERSTAND THE MATHEMATICAL PRINCIPLES BEHIND THE COSMOS? I CAN'T EVEN ADD UP A RESTAURANT BILL
RESTAURANT
BILL
CHRIS MADDEN

Today's Recipe…

- ❖ Maths and Biology
- ❖ Application of Mathematics on different Biological Problems
- ❖ Mathematical Models
- ❖ Introduction to Diseases
- ❖ Historical Perspective
- ❖ How Mathematical Principles explains the spread of Diseases
- ❖ A simple Mathematical Model
- ❖ Different Models to Fight against Diseases
- ❖ What we do…

Biology and **Mathematics** have been somewhat mutually exclusive

But the situation has substantially changed and they may study Biological Science along with Mathematics

Challenging aspects of Biological Research are stimulating innovation in Mathematics

and

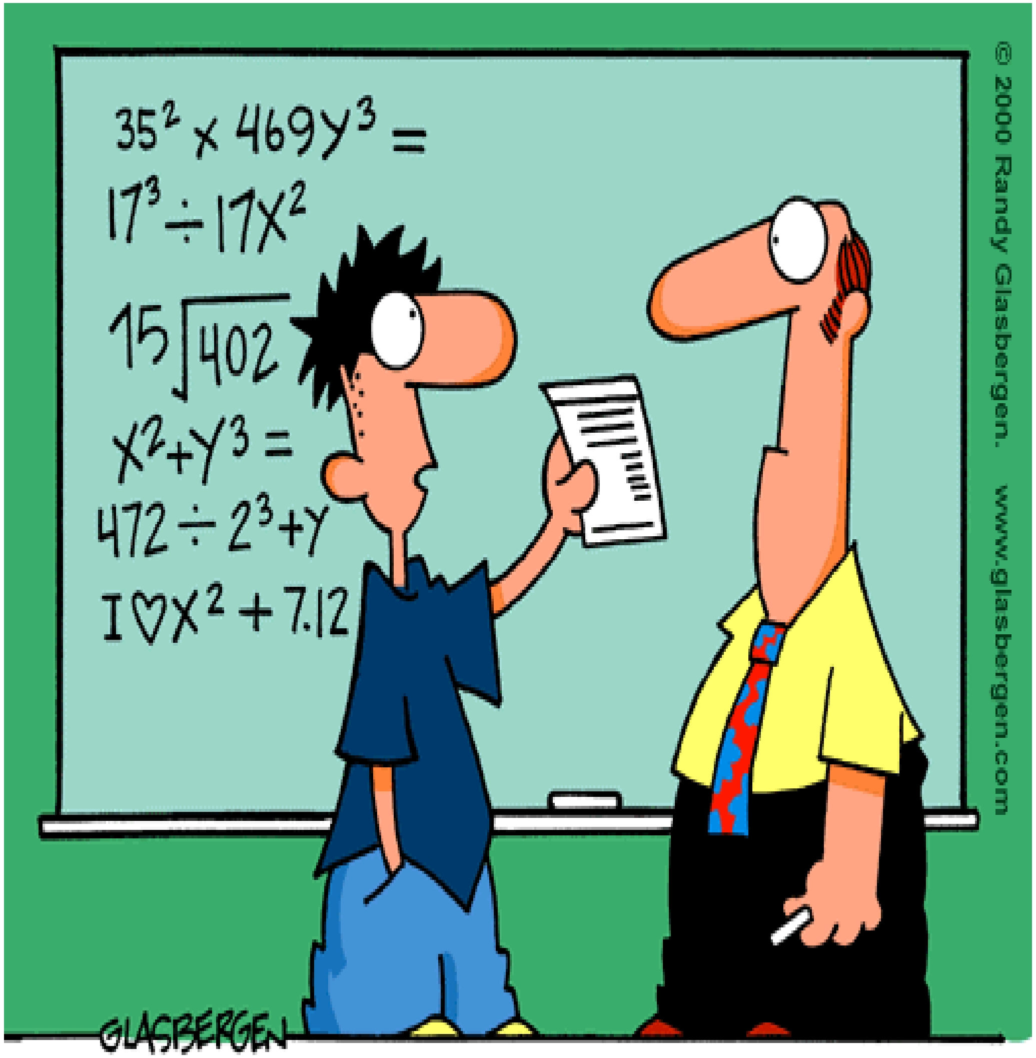
it is feasible that Biological Challenges will stimulate truly novel Mathematical Ideas as much as physical challenges have

In the common view of the sciences, **Physics** and **Chemistry** are thought to be heavily dependent on **Mathematics**

While **Biology** is often seen as a science which only in a minor way leans on quantitative methods.

A large part of the scientific community is rethinking biology education, which apparently needs to undergo mutation, one that is induced by mathematics.

Even if a biologist is missing the math gene, as this cartoon shows, one has little choice if a serious career in biology is to be made



"I HAD MY DOCTOR DO A D.N.A. BLOOD ANALYSIS. AS I SUSPECTED, I'M MISSING THE MATH GENE."

Mathematics in Physics and Biology

- Most physical processes are well described by "physical laws" valid in a wide variety of settings.
  - It is easy to get physical science models right.

- Most biological processes are too complicated to be described by simple **mathematical formulas**.
  - It is hard to get good mathematical **laws/rule/model** for biology.
  - A model that works in one setting may fail in a different setting.

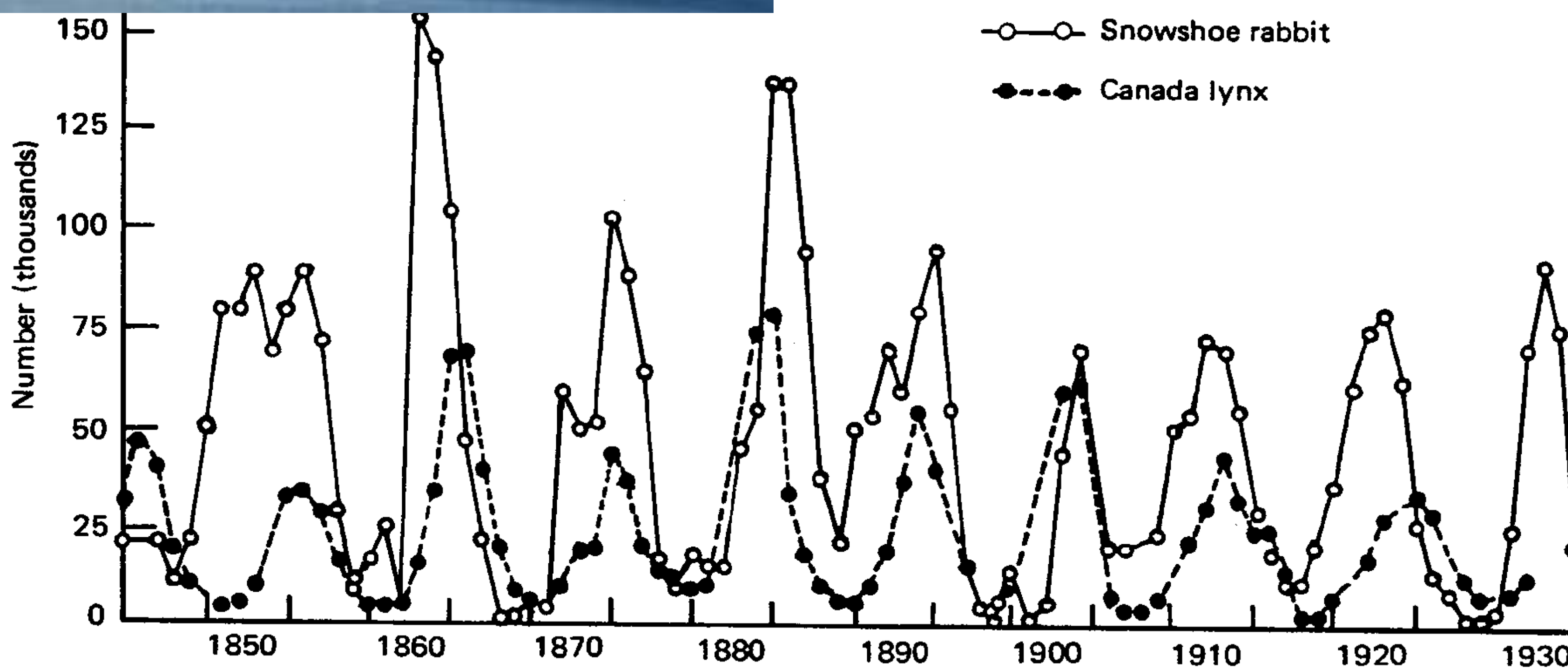
❑ **Mathematical modeling** requires good scientific intuition - Scientific intuition can be developed by observation.

❑ Detailed observation in biological scenarios can be very difficult or very time-consuming, so can seldom be done in a math course.

Mathematics Has Made a Difference

Example: Population Ecology

- Canadian Lynx and Snowshoe Rabbit
- Predator-prey cycle was predicted by a mathematical model



Classical Predator/Prey (Lynx and Rabbits)

Suppose we have a population of Lynx and a population of Rabbits,

and

We wish to build a mathematical formula to describe how the numbers of specimen in each population will change over time based on a few preliminary assumptions.

Let us make the following assumptions:

- In the absence of Lynx, Rabbits **(R)** will find sufficient food and breed without bound at a rate proportional to their population
- In the absence of Rabbits, Lynx **(F)** will die out at a rate proportional to their population
- Each Lynx/Rabbit interaction **(R-F)** reduces the Rabbit and increases the Lynx population (not necessarily equally)
- The environment doesn’t change or evolve

Classical Predator/Prey (Lynx and Rabbits)

F = number of Lynx and R = number of Rabbits

$$\Delta R = A\,R - B\,RF$$

Change in Rabbit pop. over time

Rabbit net growth

(birth - natural death)

Rabbit-Lynx interaction

(decrease due to predation)

$$\Delta F = -C\,F + D\,RF$$

Change in Lynx pop. over time

Lynx death

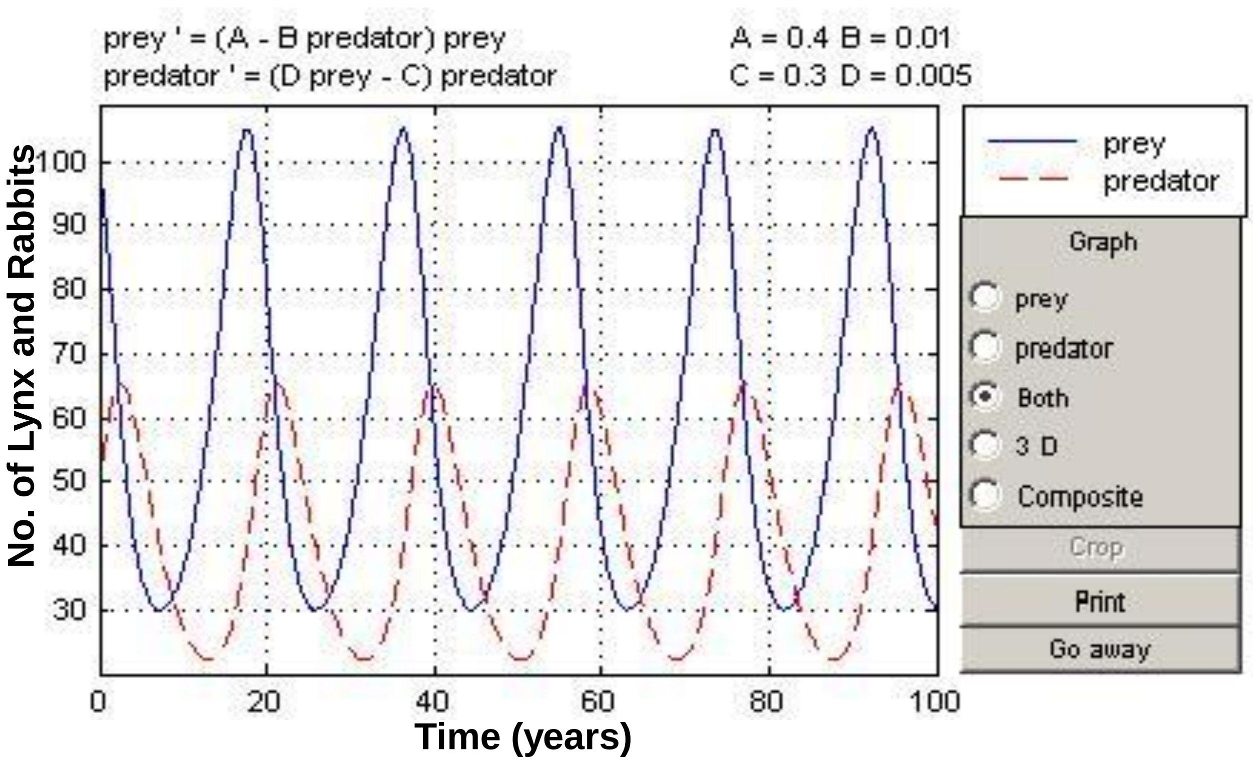
Rabbit-Lynx interaction

(increase due to predation/consumption)

A, B, C and D are constant rates

Mathematical Formula / Expression (Model)

Classical Predator/Prey (Lynx and Rabbits)



With 100 initial Rabbits and 50 initial Lynx.

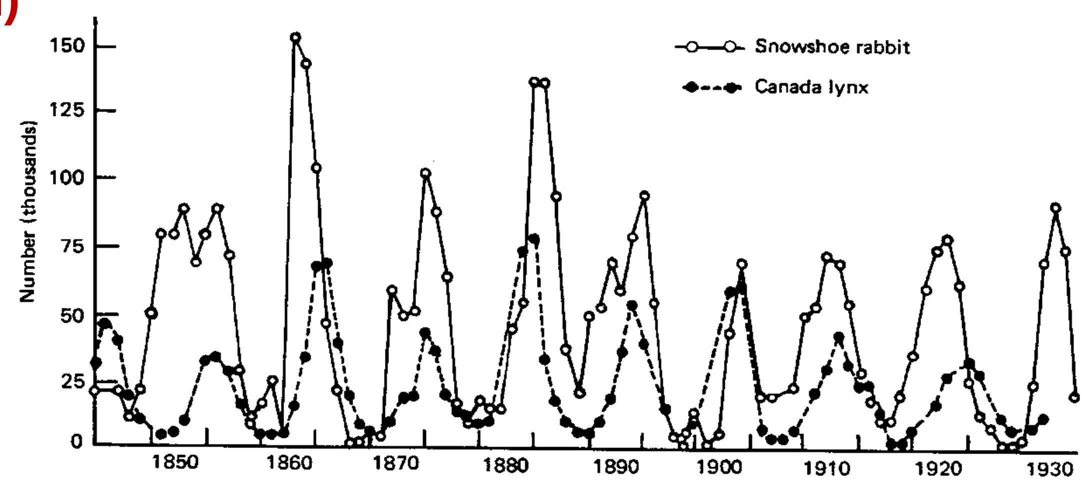
Mathematical Expression (Model)

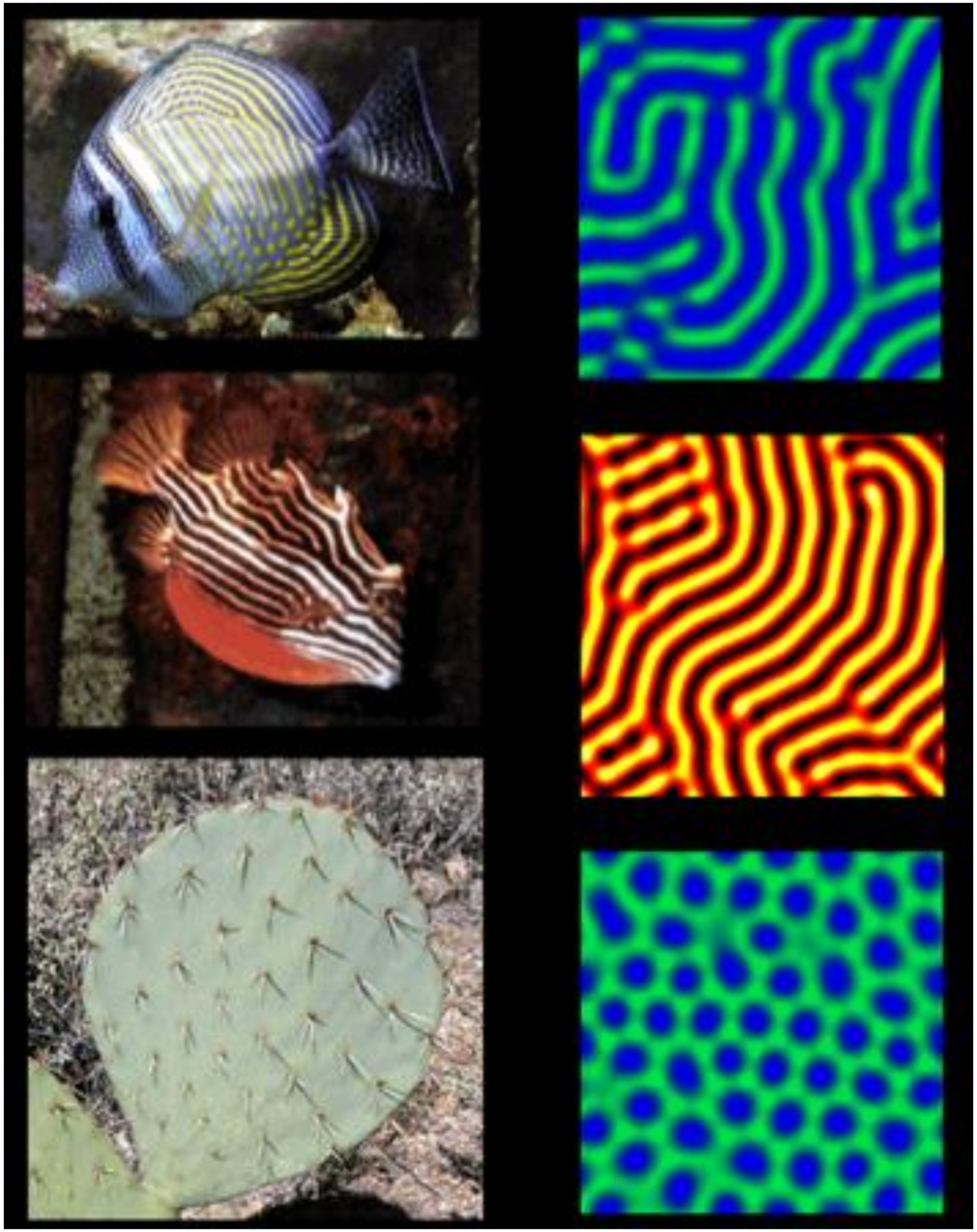
$$\Delta R = A\,R - B\,RF$$

$$\Delta F = -C\,F + D\,RF$$

F = number of Lynx

R = number of Rabbits





Patterns in Nature

- Chemicals that react and diffuse in animal coats make visible patterns
- $c(x,t)$ concentration at time t location x.

Mathematical Expression (Model)

$$\partial C/\partial t = F(C) + D\nabla^2 C$$

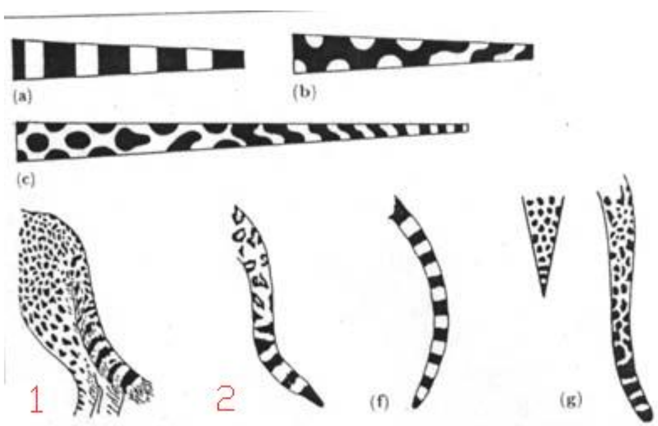
Mathematics Has Made a Difference

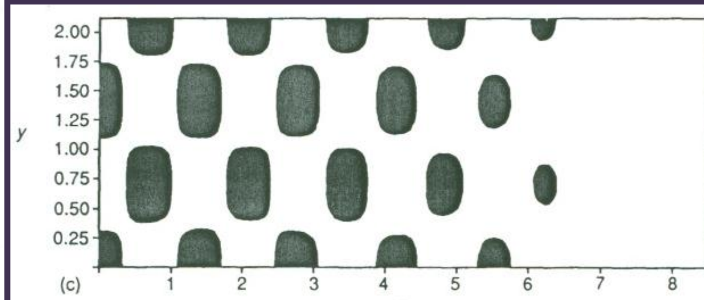
Example: Biological Pattern Formation

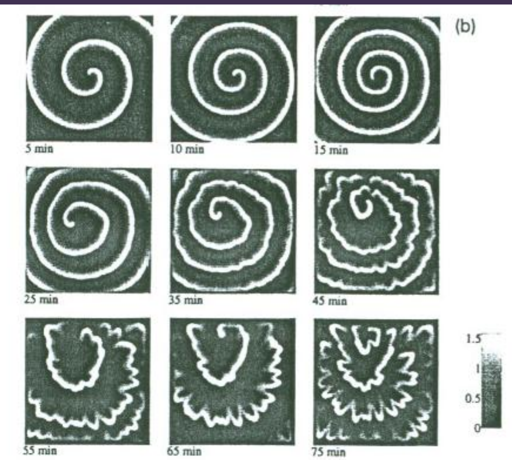
- How did the leopard / giraffe / zebra get their spots?
- Can a single mechanism predict all of these patterns?

$$\nabla^2\theta - \beta\nabla^4\theta + \nabla^2\left\{\frac{\tau n^2}{1+cn^2}\right\} = \rho\theta$$

$$\frac{\partial n}{\partial t} = D\nabla^2 n - \nabla\cdot\left(n\nabla\alpha(1-\theta)\right).$$



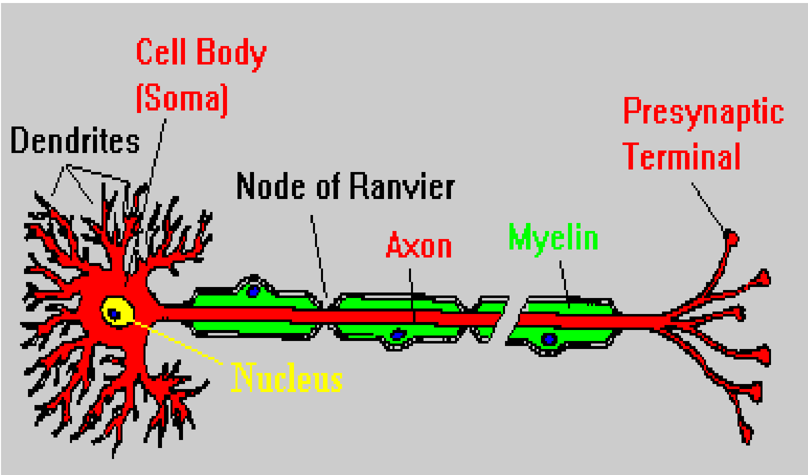


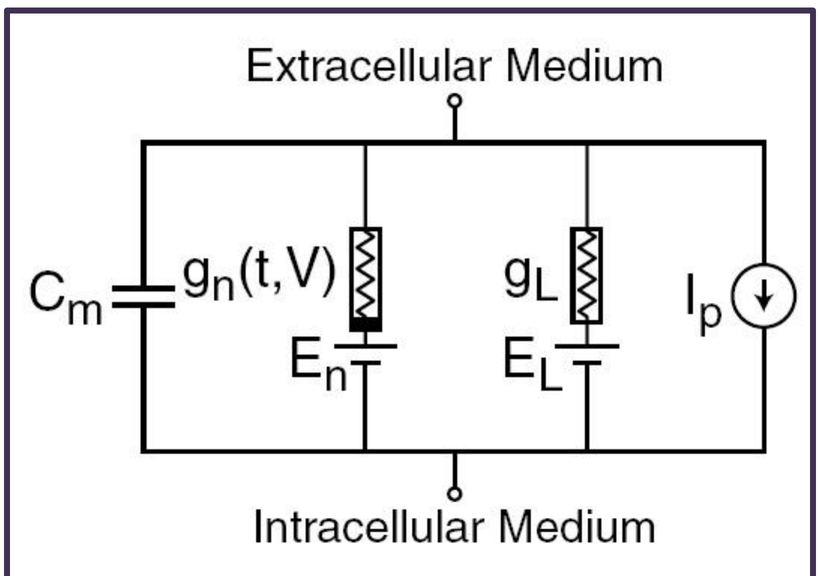


On Growth and Form: Spatio-temporal Pattern Formation in Biology.
Editor Mark A.J. Chaplain, G.D. Singh, J.C. McLachlan

Mathematics Has Made a Difference

Example: Electrophysiology of the Cell





J. Physiol. (1952) 116, 449-472

- In the 1950's **Hodgkin and Huxley** introduced and designed the first model to reproduce cell membrane action potentials
- They won Nobel Prize for this work and a new field of mathematics — excitable systems, sparked out from this

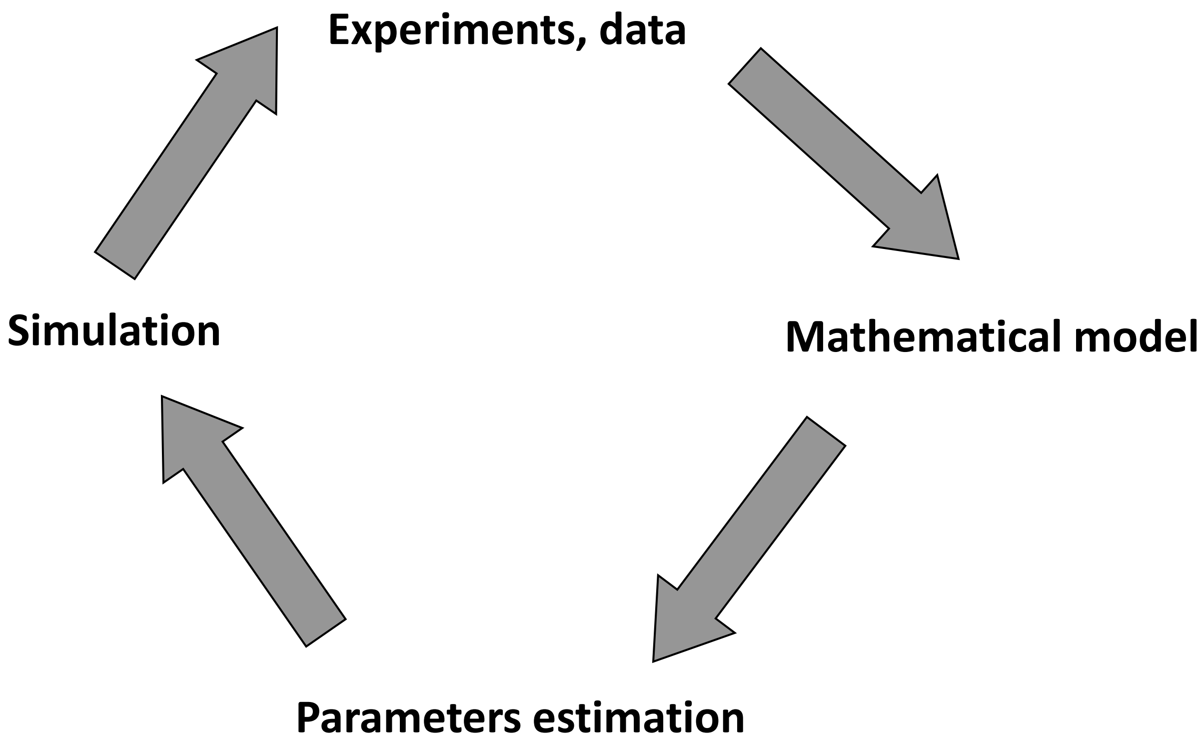
$$I_i - I'_i = I_{\mathrm{Na}} - I'_{\mathrm{Na}} = I_{\mathrm{Na}}\,(1-k).$$
$$I_{\mathrm{Na}} = (I_i - I'_i)/(1-k),$$
$$I'_{\mathrm{Na}} = k(I_i - I'_i)/(1-k),$$
$$I_{\mathrm{K}} = I'_{\mathrm{K}} = I_i - I_{\mathrm{Na}} = (I'_i - kI_i)/(1-k).$$

$$E'_{\mathrm{Na}} - E_{\mathrm{Na}} = \frac{RT}{F}\left\{\log_e \frac{[\mathrm{Na}]_i}{[\mathrm{Na}]'_o} - \log_e \frac{[\mathrm{Na}]_i}{[\mathrm{Na}]_o}\right\} = \frac{RT}{F}\log_e \frac{[\mathrm{Na}]_o}{[\mathrm{Na}]'_o}$$

Mathematical Models

Mathematical model is a well-defined **mathematical object** consisting of a collection of symbols, variables and rules (operations) governing their values.

Models are **created from assumptions** inspired by observation of some real phenomena **in the hope that the model behavior resembles the real behavior**.



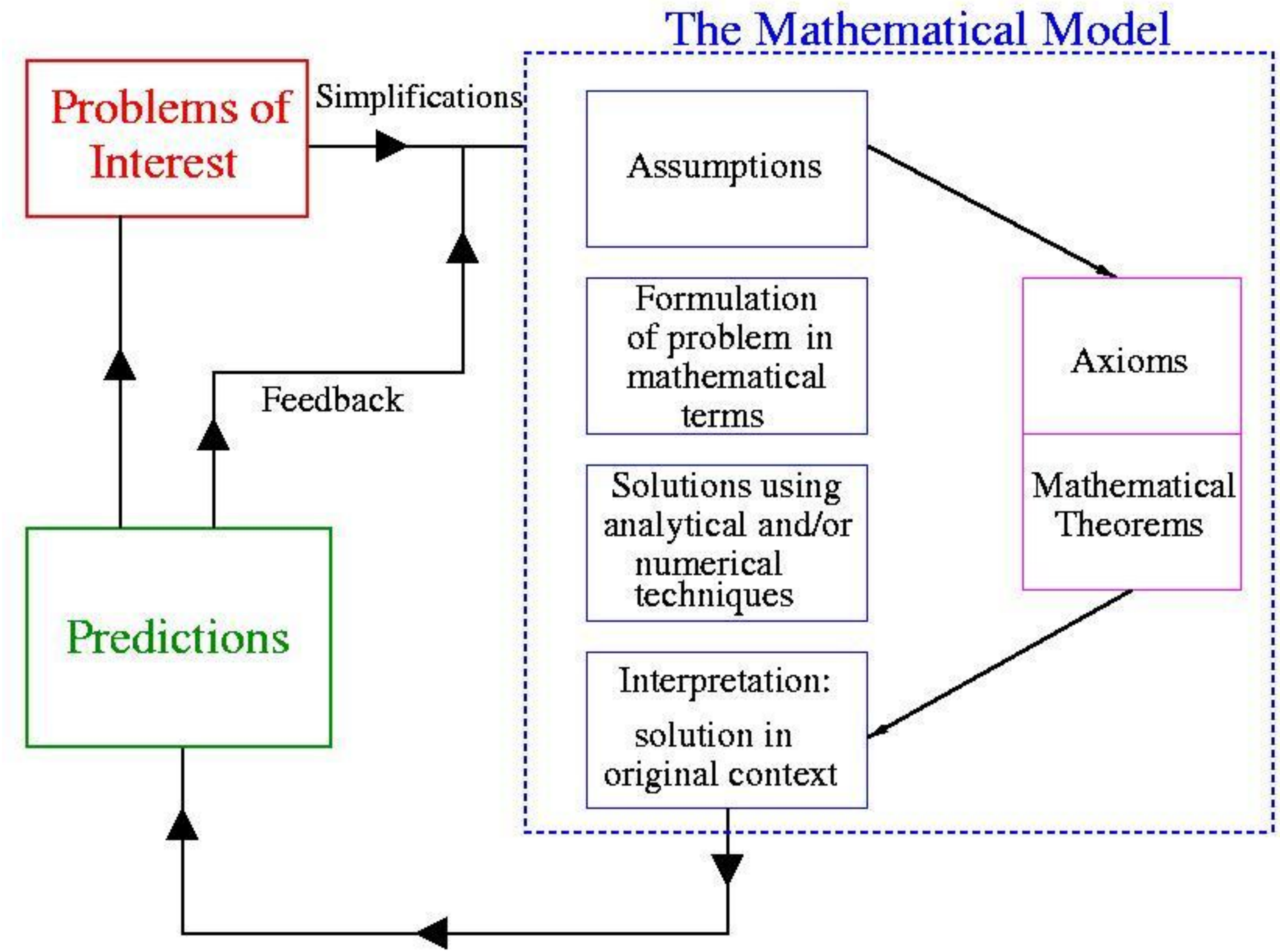
How Are Models Derived?

- Start with at problem of interest
- Make reasonable simplifying assumptions
- Translate the problem from words to mathematically/physically realistic statements of balance or conservation laws

Curve Fitting and Simulation

- Using data to obtain parameter values by **curve fitting**.
  - There is an underlying model in curve fitting or parameter determination, but the mathematical model can also be **assumed for generality**
- Using a computer to predict the behavior of some real scenario through the model **simulation**.
  - Simulation involves computation with an **assumed** model.

The Modeling Process



Why is it Worthwhile to Model Biological Systems

- To help reveal possible underlying mechanisms involved in a biological process
- To help interpret and reveal contradictions/incompleteness of data and confirm/reject hypotheses
- To predict system performance under untested conditions
- To supply information about the values of experimentally inaccessible parameters
- To suggest new hypotheses and stimulate new experiments

Some topics in Mathematical Biology

- Ecological Models **(large scale environment --- organism interplay; Structured populations; Predator-prey dynamics; Resource management)**
- Organism Models
- Large and Small Scale Models **(Epidemiology/Disease)**
- Cellular Scale **(Wound healing; Tumor growth; Immune System)**
- Quantum/molecular Scale **(DNA sequencing; Neural networks)**
- Pharmacokinetics **(Target Identification; Drug Discovery)**

Some interesting current studies

- *The effect of bacteria on wound angiogenesis*
- *Zoonotic diseases carried by rodents: seasonal fluctuations*
- *Computational modeling of tumor development*
- *Hepatitis B disease spread*
- *System Biology*

Now Diseases…………

What is disease?

Disease is a disorder or malfunction of the mind or body, which leads to a departure from good health.

Can be a disorder of a **specific tissue** or **organ** due to a **single cause.** E.g. Measles, Chicken Pox, Malaria, HIV etc.

May have many causes.
Often referred to as **multifactorial.** E.g. heart disease.

Measles

Chickenpox

Acute disease

Sudden and rapid onset

Symptoms disappear quickly

E.g. Influenza

Chronic disease

Long term

Symptoms lasting months or years

E.g. Tuberculosis

Categories of diseases

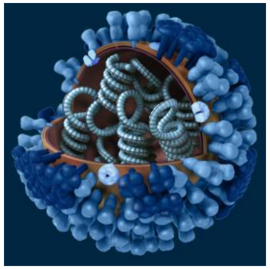
Physical disease

Results from permanent or temporary damage to the body

Infectious diseases

Organisms that cause disease inside the human body are called **pathogens**

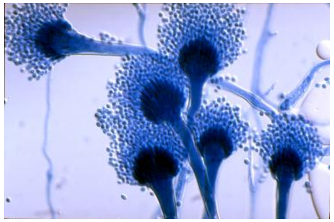
Mycobacterium Tuberculosis



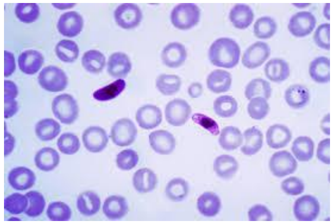
Influenza virus

Bacteria and **Viruses** are the best known pathogens.

Fungi, **protozoa** and **parasites** can also cause diseases



Aspergillus fumigatus

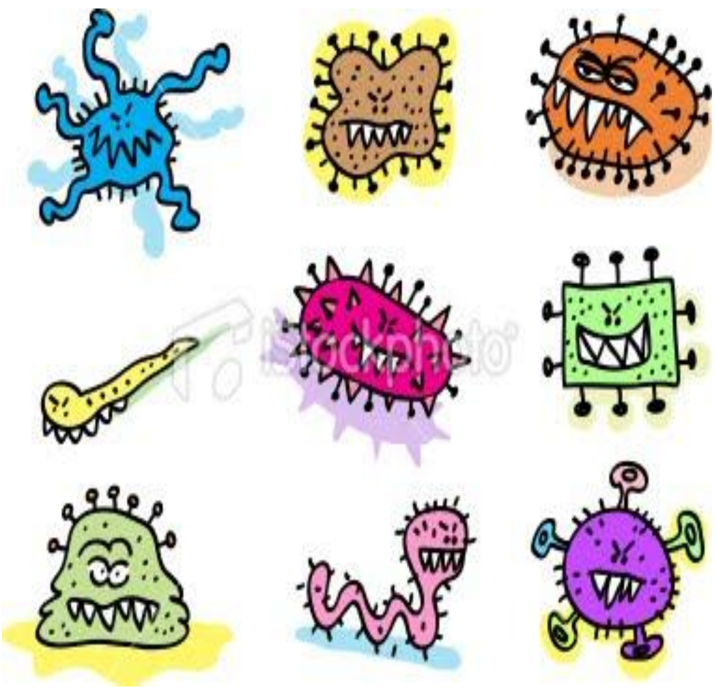


Plasmodium falciparum

Diseases are said to be infectious or communicable if pathogens can be passed from one person to another.

Infectious Diseases Are Big Problems

Infectious diseases are big problems in India and worldwide, for people of all ages, as well as for livestock.



2005: More than 130,000 cases of cholera occur worldwide

2006: More than 350,000 cases of gonorrhea are reported in the United States

2007: 33.2 million people worldwide have HIV infections

2000-2012: On an average **2% of the entire population** of India tested positive for Malaria,

2012: Total new and relapse cases of **TB – 12,89,836**; Total cases notified-**14,67,585**

Each year in the United States, 5% to 20% of the population gets the flu and 36,000 die

Source: World Health Organization (http://www.who.int/en/)

Historical perspective

❑ **The Antonine Plague, 165–180 AD, was an ancient pandemic, either of smallpox or measles, brought back to the Roman Empire by troops returning from campaigns in the Near-East -**

Invaded the Roman Empire, claimed lives of two Roman emperors and caused drastic population reduction and economic hardships [Wikipedia (2008)].

❑ **In the early 1500s, smallpox was introduced into the Caribbean by the Spanish armies led by Cortez, from where it spread to Mexico, Peru, and Brazil**

- One of the factors that resulted in widespread deaths among the **Incas**.
- The population of Mexico was reduced from 30 million to less than 2 million during a period of 50 years after the Spanish invasion [*Brauer and Castillo-Chavez (2001)*]

❑ **The Black Death (bubonic plague) had spread four times in Europe**

- Death of more than 10 000 people every day in 600 AD, and death of as much as one-third of the population between 1346 and 1353.
- The disease recurred regularly in various parts of Europe and, led to the death of one-sixth of the population in London between 1665 and 1666.

Source: Wikipedia

- Great progresses had been achieved, especially during the 20th century

- While **smallpox** outbreaks have occurred from time to time for thousands of years, the disease is now eradicated after a successful worldwide vaccination program [HHS (2008)].

- In 1991,World Health Assembly passed a resolution to eliminate **leprosy** - The target was achieved on time [WHO (2008)].

- **Poliomyelitis (polio)** - the Global Polio Eradication Initiative was launched in 1988, Internationally coordinated public health project to date

  — In 2006, less than 2000 cases were reported [WHO (2008)].

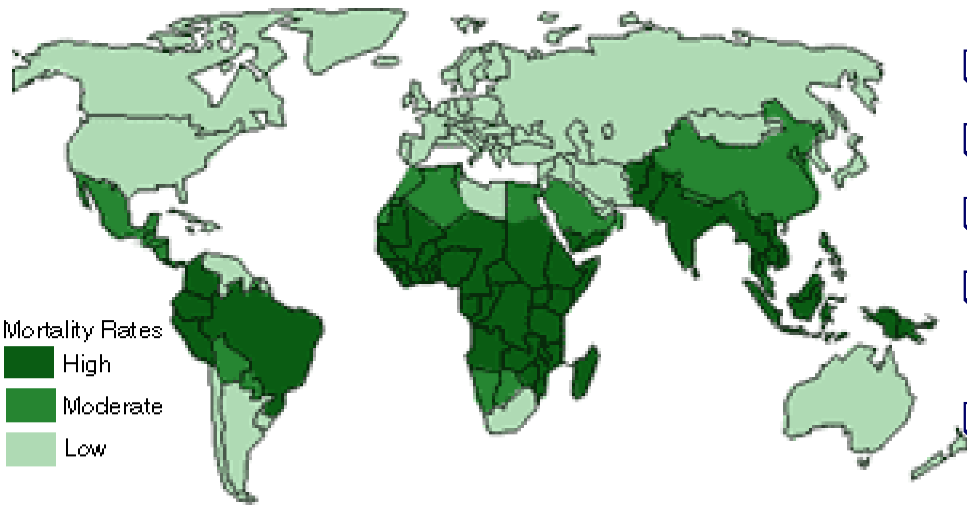
- Some other infectious diseases, such as **diphtheria**, **measles**, **pertussis**, and **tetanus** (lockjaw), have been significantly under control in many countries.

- **While the great achievement and progresses in the prevention and control of infectious diseases are promising and inspiring, there is a long way to go to completely eradicate infectious diseases in the world.**

- An estimated 1.5 million people died from **tuberculosis** in 2006 [WHO (2007)].

- **Malaria** - the world's most important tropical parasitic disease.

  Approximately, 40% of the world's population, mostly those living in the world' poorest countries, are at risk of malaria.



Global Statistics

- 40% of the world's population is at risk
- 300-500 million new cases/year
- 1.5-2.7 million deaths/year
- Malaria is endemic to over 100 countries and territories
- More than 90% of all cases are in sub-Saharan Africa

In addition to frequently occurring disease epidemics, the threat of emergence or
re-emergence of new epidemics continues to be a concern for policy makers and the public health services.

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News and top stories

Working with communities is the key to stopping Ebola

When Dr Peter Clements arrived in Lofa County, Liberia eight weeks ago, from the WHO country office in Monrovia, 20-30 patients were arriving at the MSF hospital with Ebola-like symptoms every day. People living in the community were afraid, civil unrest was simmering, and an ambulance and health workers were being targeted. Although UN security advised him not to, Dr Clements traveled the 12 hours over dirt roads to the area nearest the Guinea border. Once there, he walked into the hostile communities and went straight to the chiefs.

WHO

Read the full story

Ebola response | Liberia health worker training | Antenatal care | Age-friendly world

Faces of the Ebola outbreak response

10 October 2014 -- As soon as the Ministry of Health of Democratic Republic of Congo notified WHO of an Ebola outbreak in the Equateur Province of the country, WHO deployed a team of experts to the affected area. Watch how WHO and partners are working around the clock to help people get medical care that can save lives. Browse the photo gallery that tells the stories of people contributing to contain the Ebola outbreak in West Africa. Our highest gratitude for their hard work and dedication.

- Photo gallery: Faces of the Ebola outbreak response
- Video: Ebola outbreak response in DRC

Ebola outbreak

Ebola virus disease - web site

Evolution of Ebola response - 9 essays

Situation assessments

Ebola response roadmap

Situation reports on Ebola response roadmap

Ebola vaccines, therapies, and diagnostics

Ebola: What you need to know

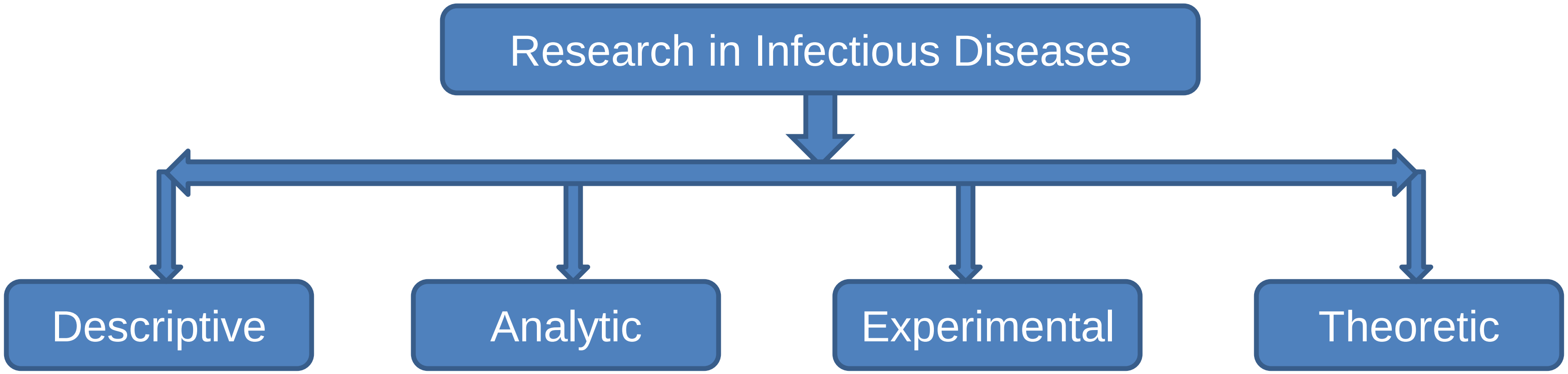
TRAVEL TO AND FROM EBOLA-AFFECTED COUNTRIES IS LOW-RISK HERE IS WHAT YOU NEED TO KNOW

WHILE TRAVELLING

AT AIRPORTS AND AT YOUR DESTINATION

World Health Organization

- What you need to know when you are travelling
- Protective measures for medical staff
- Protective measures for general public



- **Epidemic dynamics study is an important theoretic approach to investigate the transmission dynamics of infectious diseases**

  It formulates mathematical models to describe the mechanisms of disease transmissions and dynamics of infectious agents.

- **Mathematical models** are based on **population dynamics**, **behavior of disease transmissions**, **features of the infectious agents**, and **connections** with other **social** and **physiologic factors**.

Mathematical models give good understanding of how infectious diseases spread, and identify more important and sensitive parameters, make reliable predictions and provide useful prevention and control strategies and guidance.

Help us to make more realistic simulations and reliable long-term transmission prediction which may not be feasible by experiments or field studies.

“ **Modeling can help to ...**

Modify vaccination programs if needs change
Explore protecting target sub-populations by vaccinating others
Design optimal vaccination programs for new vaccines
Respond to, if not anticipate changes in epidemiology that may accompany vaccination
Ensure that goals are appropriate, or assist in revising them
Design composite strategies,… ”

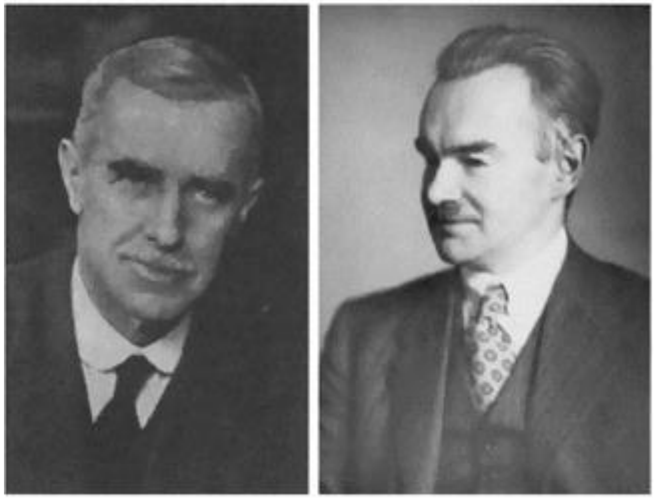
Walter Orenstein,
Former Director of the National Immunization Program in the Center for Diseases Control (CDC)

- Mathematical modeling of infectious diseases can be traced back to 1760 when Bernoulli used mathematical models for smallpox [**Bernouilli** (1760)],

- 20th century: **Hamer** formulated a discrete-time model for the spread of measles in 1906.

- **Sir Ronald Ross** (1911) - transmissions of malaria between human beings and mosquitoes , and determined a threshold of the size of mosquitoes below which the spread of malaria can be controlled. (Second Nobel Prize in Medicine)

- **Kermack and McKendrick** formulated a well-recognized **SIR** (susceptible–infective–recovered) compartmental model, in 1926, to study the outbreak of Black Death in London during the period of 1665–1666, and the outbreak of plague in Mumbai in 1906.



- They later, in 1932, formulated an **SIS** compartment model and, formally introduced the concept of thresholds that determines whether a disease spreads in a given population

•More intensive studies on epidemic dynamics took place after the middle of the 20th century.

• A landmark publication is the book by **Bailey** (first edition in 1957; second edition in 1975)

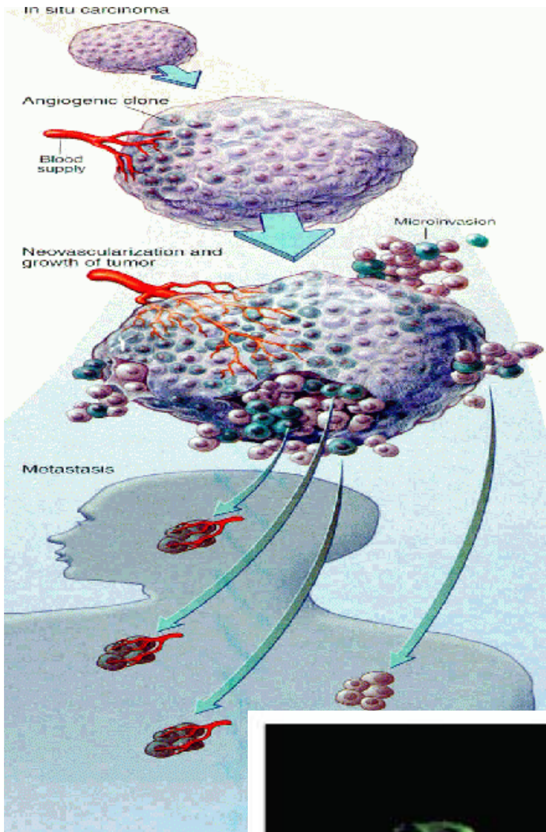
• **More developments and progresses - during the past 20 years.**

• Massive mathematical models have been formulated and developed to study various infectious diseases, ranging **from more theoretic to**

> **general ones** [Waltman (1974); Burnett and White (1974); Hoppensteadt (1975); Frauenthal (1980); Anderson and May (1982); Evans (1982); Webb (1985); Kranz (1990); Busenberg and Cooke (1993); Capasso (1993); Isham and Medley (1996); Daley and Gani (1999); Diekman and Heesterbeek (2000)]
>
> **more specific ones** e.g. measles, malaria, tuberculosis, sexually transmitted diseases (STD), or AID/HIV [Hethcote and Yorke (1984); Hethcote (2000); Hyman and Stanley (1988); Brauer and Castillo-Chavez (2001); Brauer *et al. (2008)].*

Modeling Has Made A Difference

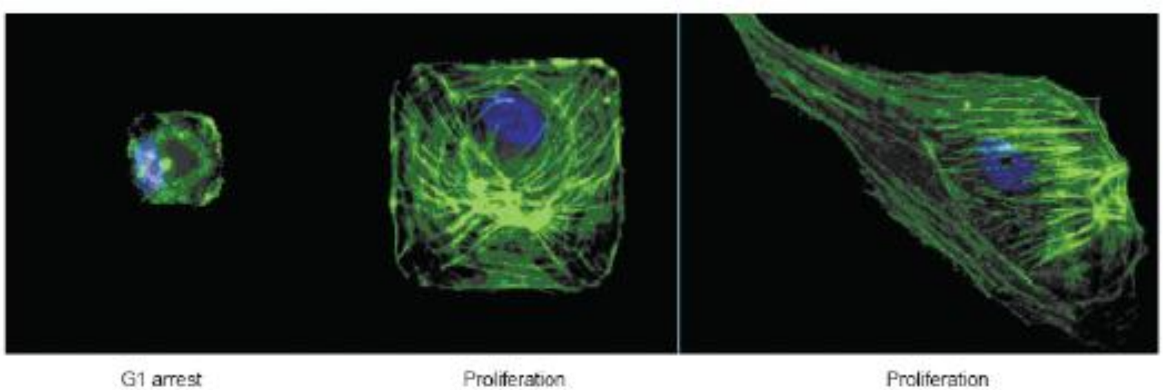
Example: Tumor Growth

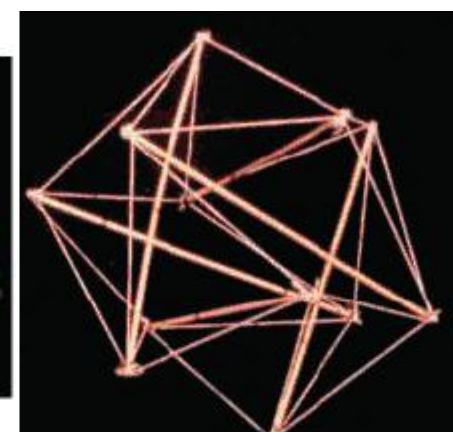


- Mathematical models have been developed that describe tumor progression and help predict response to therapy.

$$\frac{\partial n}{\partial t} + \nabla \cdot (\mathbf{v}_n n) = \nabla \cdot (D \nabla n) + \lambda(n, C_i) - \mu(n, C_i),$$

$$\frac{\partial m}{\partial t} + \nabla \cdot (\mathbf{v}_m m) = \mu(n, C_i),$$





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Let us try to understand a mathematical model……

Spread of Infection in a population

Infectious Disease Epidemiology

Epidemiology

- **Deals with one population**
- **Risk ➔ case**
- **Identifies causes**

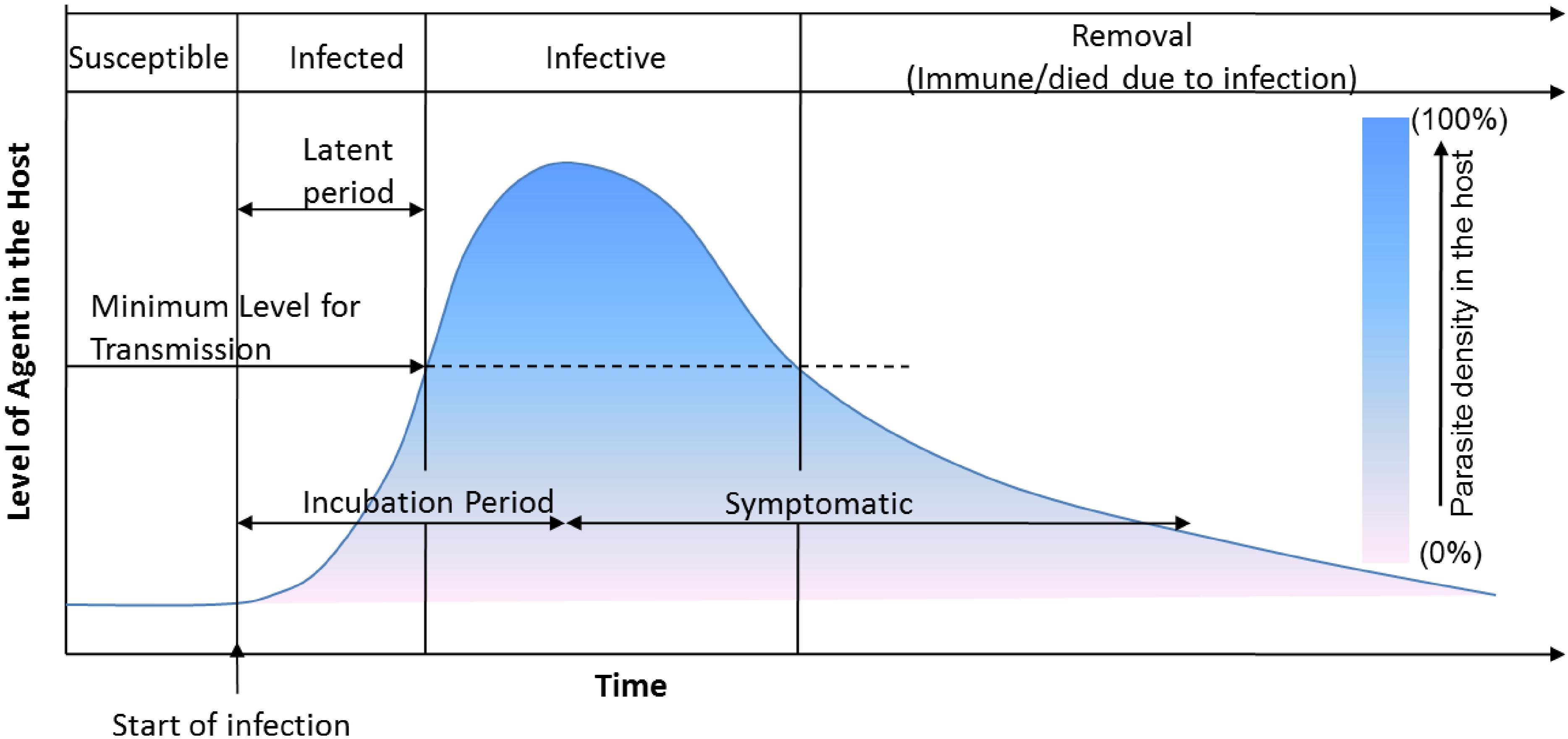
Infectious disease epidemiology

- ❖ Two or more populations ➡
- ❖ A case is a risk factor ➡
- ❖ The cause often known ➡

Two or more populations

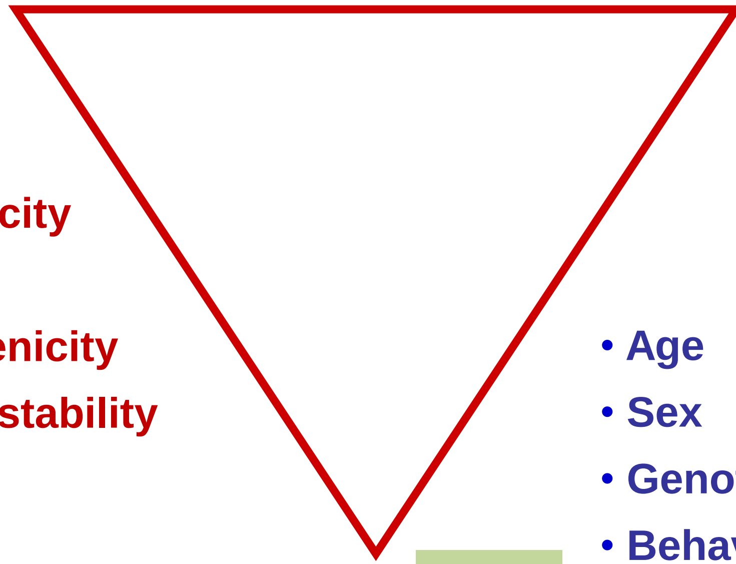
- ❖ **Humans**
- ❖ **Infectious agents**
  - ❖ **Helminths, bacteria, fungi, protozoa, viruses, prions**
- ❖ **Vectors**
  - ❖ **Mosquito (protozoa-malaria), snails (helminths-schistosomiasis), Sand Fly (Leishmania-KalaAzaar)**
- ❖ **Animals**
  - ❖ **Dogs and sheep/goats – *Echinococcus***
  - ❖ **Mice and ticks – *Borrelia***

Timeline for Infection



Transmission

Factors Influencing Disease Transmission



Agent

- Infectivity
- Pathogenicity
- Virulence
- Immunogenicity
- Antigenic stability
- Survival

Environment

- Weather
- Housing
- Geography
- Occupational setting
- Air quality
- Food

Host

- Age
- Sex
- Genotype
- Behaviour
- Nutritional status
- Health status

Epidemiologic Triad-Related Concepts

Infectivity (ability to infect)

(number infected / number susceptible) x 100

Pathogenicity (ability to cause disease)

(number with clinical disease / number infected) x 100

Virulence (ability to cause death)

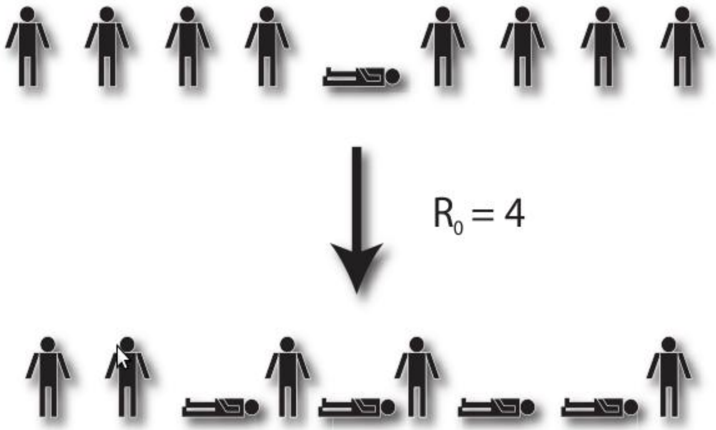
(number of deaths / number with disease) x 100

All are dependent on host factors

All are numbers………….**MATH** Again…

Calculation of the Basic Reproductive Ratio, R_0

For a microparasitic infection, R_0 is more preciously defined as the average number of secondary infections produced where one infected individual is introduced into a host population, where everyone is susceptible.



Graphical illustration of the basic reproductive rate R_0. Here a sick individual is placed into an otherwise susceptible population of 9 individuals. Over the entire duration that this individual is infected, she or he infects 4 other individuals. Thus the basic reproductive rate here is 4.

Definitions

Epidemic

Outbreak of an infectious disease affecting a disproportionately large number of individuals in a population, community, or region within a short period of time

Pandemic

Spread of an epidemic to a large region (or worldwide)

Endemic

An infectious disease is endemic when it is maintained in a population without the need for external inputs

Transmission Factor R_0

(of the microparasite, also: basic reproduction number)

Infected primary individual is placed in a large susceptible population
R_0: average number of secondary individuals infected by one primary case
(applicable in the early stages of an epidemic)

$R_0 > 1$ **Epidemic** $R_0 = 1$ **Endemic** $R_0 < 1$ **Eradication**

Effective transmission factor (if a fraction p is immune): $R_{\text{eff}} = R_0(1-p)$

Critical fraction of the population that has to be immune to prevent epidemic

$$R_{\text{eff}} < 1 \longrightarrow p > 1 - \frac{1}{R_0}$$

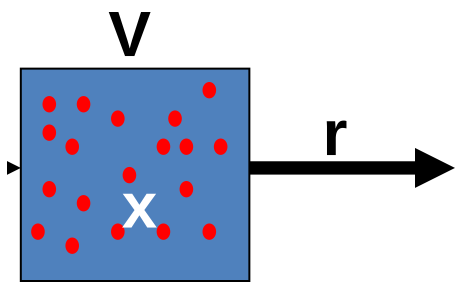
Typical Transmission Factors

Infectious Disease	R_0	$p_{(min)}$
Smallpox	3-5	70-80%
Measles	10-20	90-95%
Malaria	(100)*	99%

*Malaria needs specific "external" vector (mosquito) for transmission

Current level of U.S. population immune against smallpox: about 18%
(growth rate of epidemic today would be much higher than those of historical smallpox epidemics)

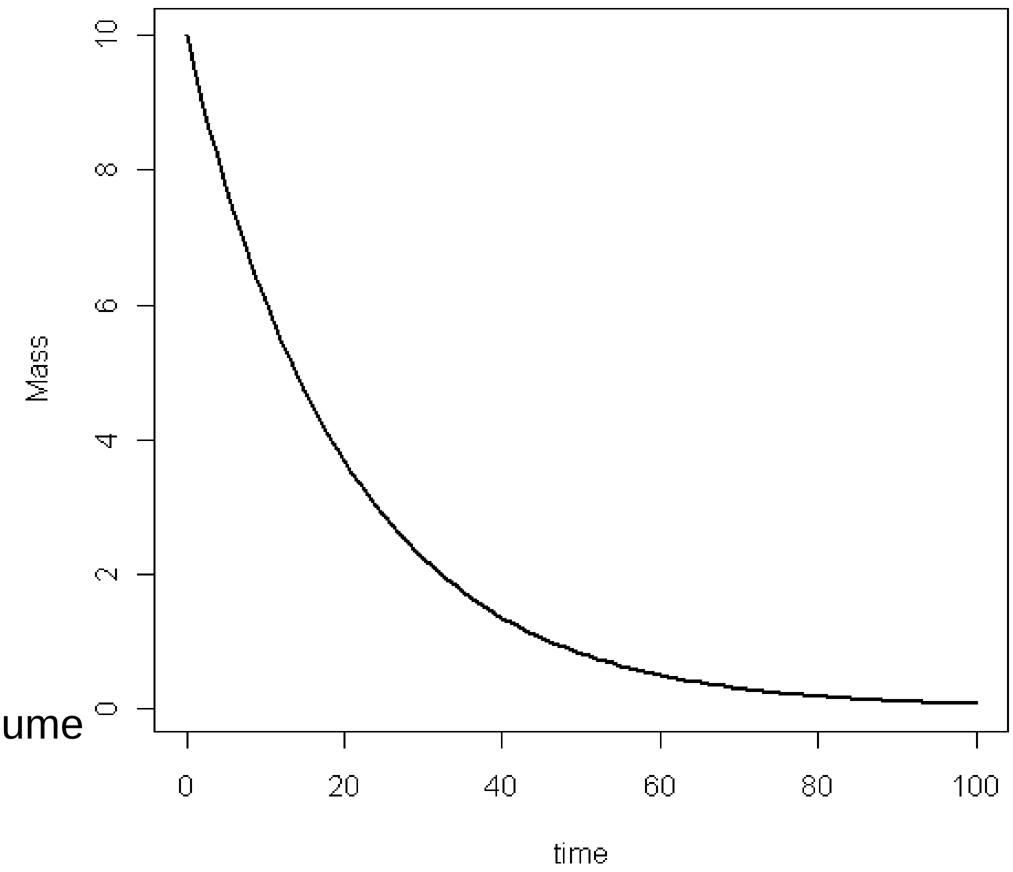
A First Model



$$\frac{\text{Change}}{\text{Time}} \propto \text{Density}$$

$$\frac{\text{Change}}{\text{Time}} \propto \rho$$

In this case: LOSS @ r; Density = Mass/Volume



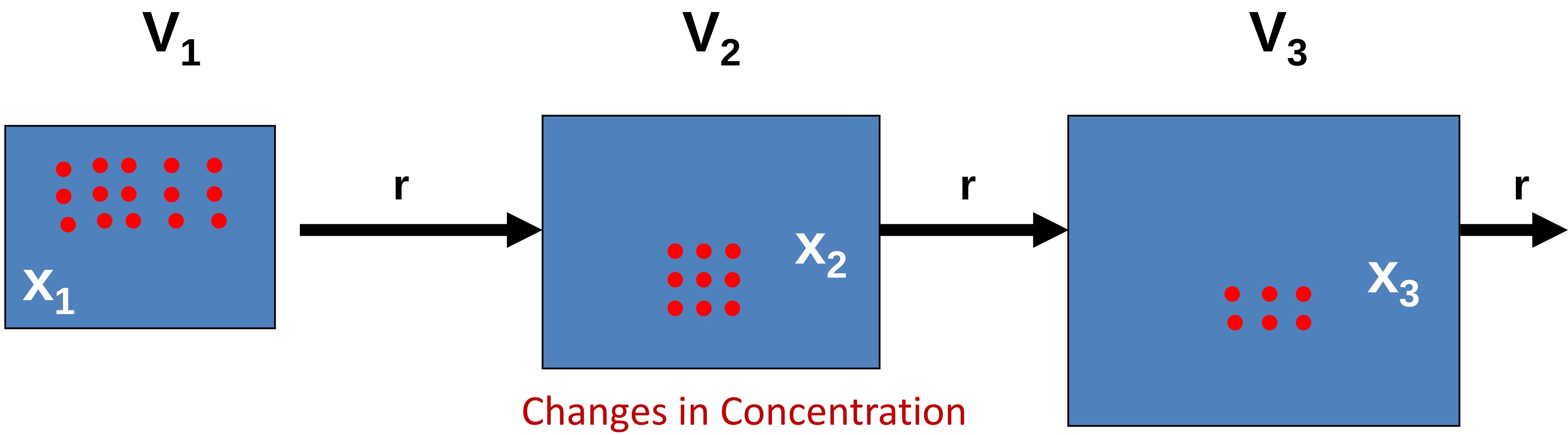
$$\frac{Change}{Time} = -r\frac{x}{V}$$

$$\frac{dx}{dt} = -r\frac{x}{V}$$

$$x(t) = x(0)e^{-(r/V)t}$$

e is an important mathematical constant (Approx. = 2.71828)

Compartments & Flow



Changes in Concentration

$$\frac{Change\ in\ 1st\ Vessel}{Time} = Loss\ in\ density = -r\frac{x_1}{V_1}$$

$$\frac{Change\ in\ 2nd\ Vessel}{Time} = Gain\ \ from\ 1st - Loss\ in\ density = r\frac{x_1}{V_1} - r\frac{x_2}{V_2}$$

$$\frac{Change\ in\ 3rd\ Vessel}{Time} = Gain\ \ from\ 2nd - Loss\ in\ density = r\frac{x_2}{V_2} - r\frac{x_3}{V_3}$$

Mathematical Expression (Model)

$$\frac{dx_1}{dt} = -r\frac{x_1}{V_1}$$

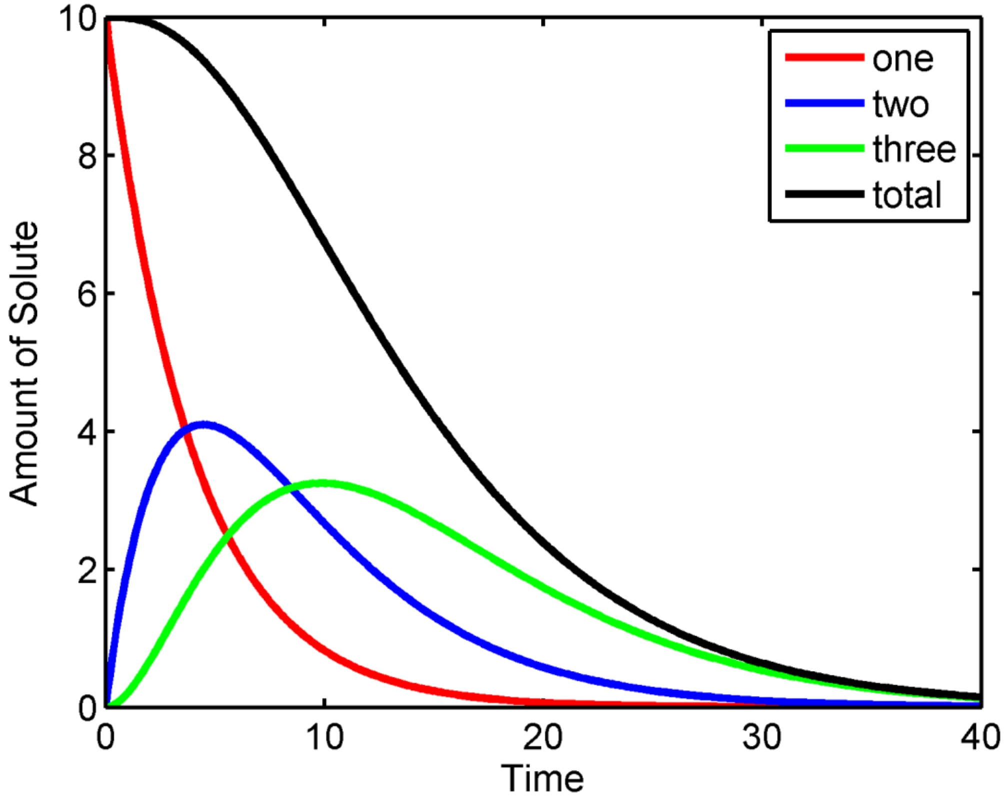
$$\frac{dx_3}{dt} = r\frac{x_2}{V_2} - r\frac{x_3}{V_3}$$

$$\frac{dx_2}{dt} = r\frac{x_1}{V_1} - r\frac{x_2}{V_2}$$

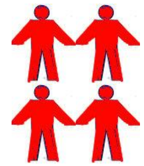
Evaluate the Model

- **Choose some parameters**
  - $V_1 = 80$
  - $V_2 = 100$
  - $V_3 = 120$
  - $r = 20$
- **Define the initial conditions**
  - $x_1(0) = 10$
  - $x_2(0) = 0$
  - $x_3(0) = 0$

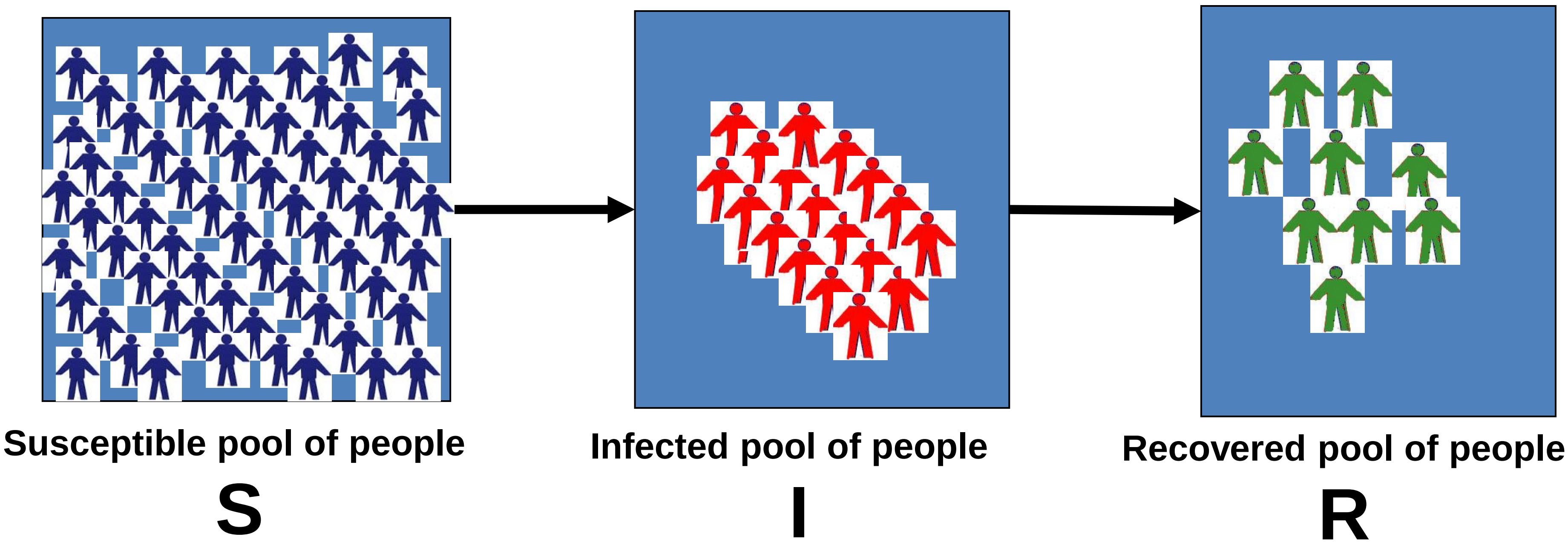
Results



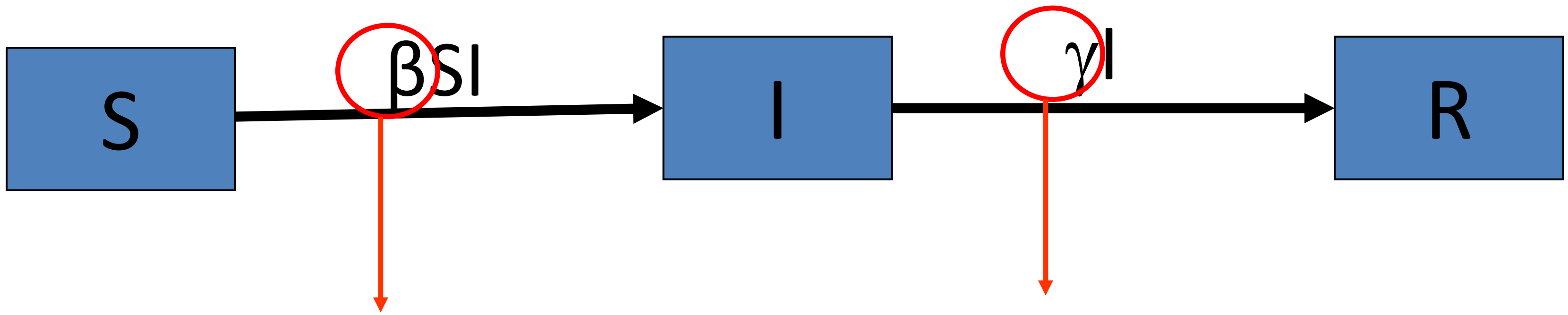
http://math.fullerton.edu/mathews/N310/projects2/p14.htm (read from "More Background" onwards)



Infected Individuals



Basic Model for Infectious Disease



Infection Rate:

Contact rate

Infection probability

Recovery Rate

If D is the duration of infection:

γ = 1/D

$$\frac{\text{Change in } S}{\text{Time}} = \frac{dS}{dt} = -\beta SI$$

$$\frac{\text{Change in } R}{\text{Time}} = \frac{dR}{dt} = \gamma I$$

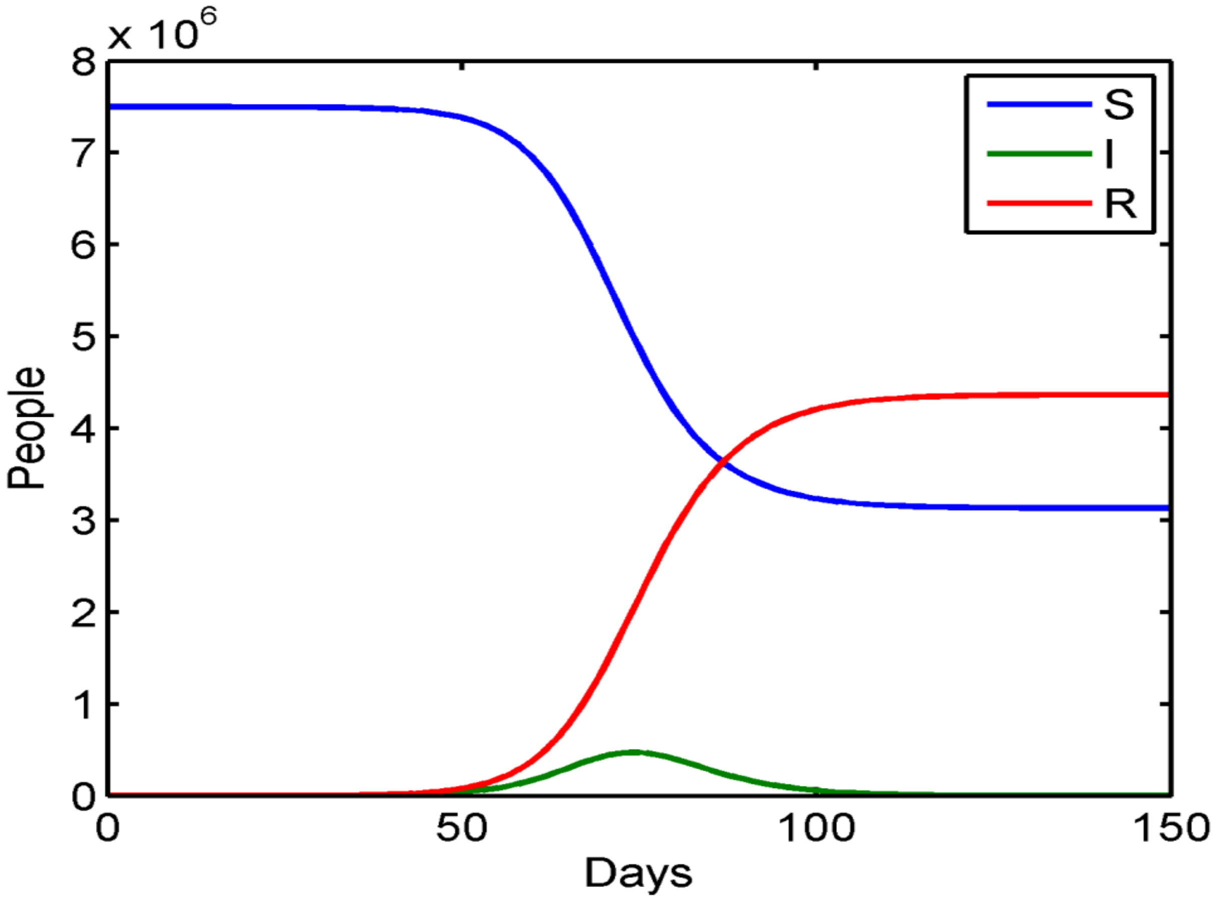
$$\frac{\text{Change in } I}{\text{Time}} = \frac{dI}{dt} = \beta SI - \gamma I$$

Kermack–Mckendrick SIR compartment model

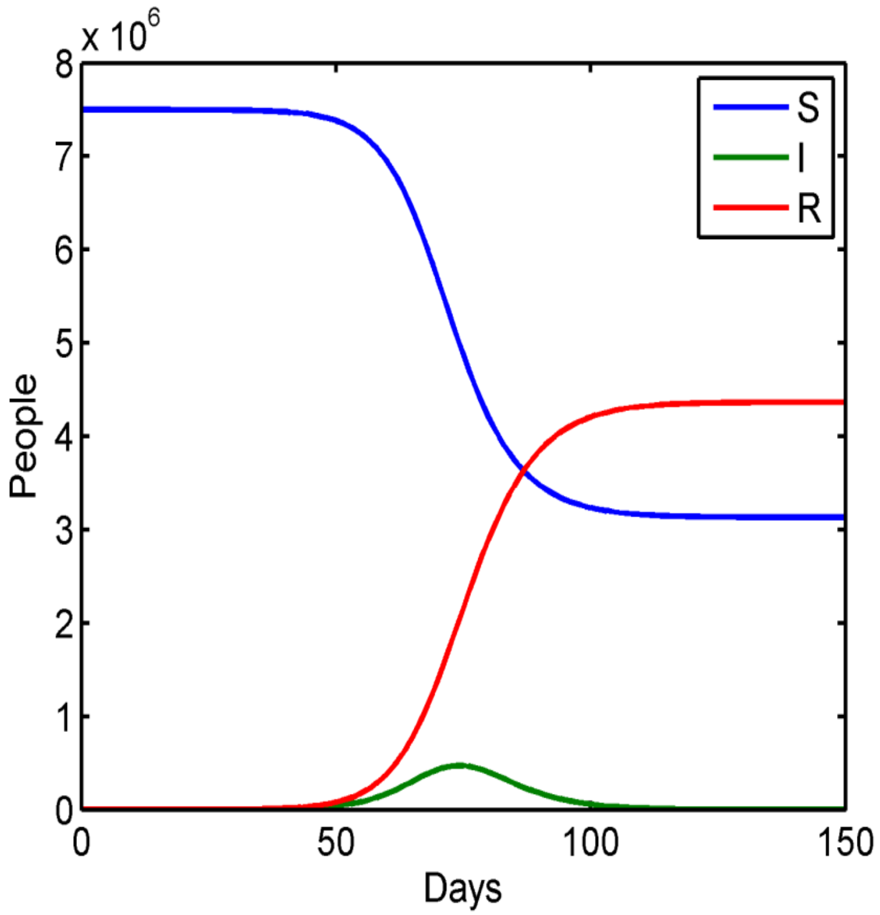
For viral diseases, such as influenza, measles, and chickenpox, the recovered individuals, in general, gain immunity to the same virus.

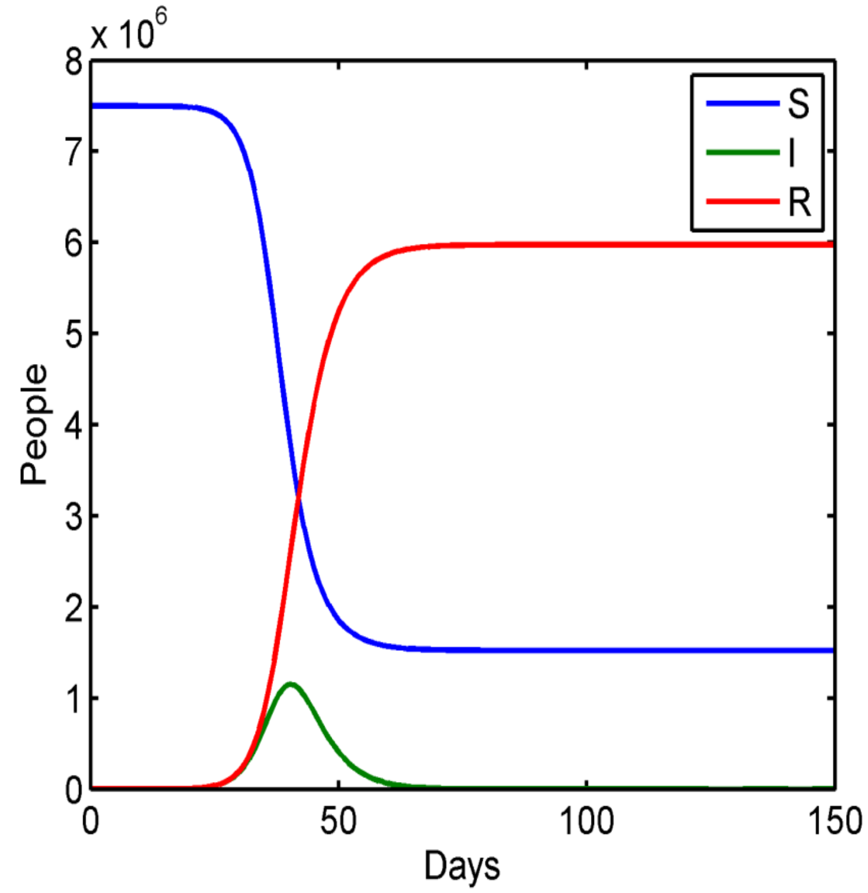
A "typical" flu epidemic

- Each infected person infects a susceptible every 2 days so β =1/2
- Infections last on average 3 days so γ =1/3
- London has 7.5 million people
- 10 infected people introduced



Changes to Infection Rate





$\beta = 1/2$

$\gamma = 1/3$

$\beta = 1/1.5$

$\gamma = 1/3$

Let us calculate the Basic Reproduction Number, R_0

$$R_0 = \beta \frac{1}{\gamma} S_0 = \frac{S_0}{\rho}, \qquad \rho = \frac{\gamma}{\beta}$$

S_0 = Initial Susceptible Population
β= Rate of Infection
γ= Rate of Recovery

the epidemic spreads when *$R_0 > 1$ and dies out when $R_0 < 1$.*

Most of the cases, **β and γ,** are unknown

Alternative way to calculate, ρ

FIND: K = $S_0 + I_0$

S_0 = Initial Susceptible Population
I_0 = Initial Infected Population

FIND: S_∞ **S_∞ =** Final Susceptible Population OR Number of Survival

MATH AGAIN…..CALCULATE:

$$K - S_\infty + \rho \ln \frac{S_\infty}{S_0} = 0.$$

ln(*x*) *is called* **natural logarithm** of a number x. For example: ln(2) is 0.69314..., because $e^{0.69314...} = 2$, ***e*** is an important mathematical constant (Approx. = 2.71828)

Example: The village of Eyam near Sheffield, England suffered an outbreak of bubonic plague in 1665–1666 [Brauer and Castillo-Chavez (2001)]. Preserved records show that the initial numbers of susceptibles and infectives were 254 and 7 in the middle of May 1666, respectively. and only 83 persons survived in the middle of October 1666.

The parameters can be estimated as

$$S_0 = 254,\ I_0 = 7,\ S_\infty = 83,$$

$$K = S_0 + I_0 \quad \boxed{= 261,}$$

so that

$$\rho = 153$$

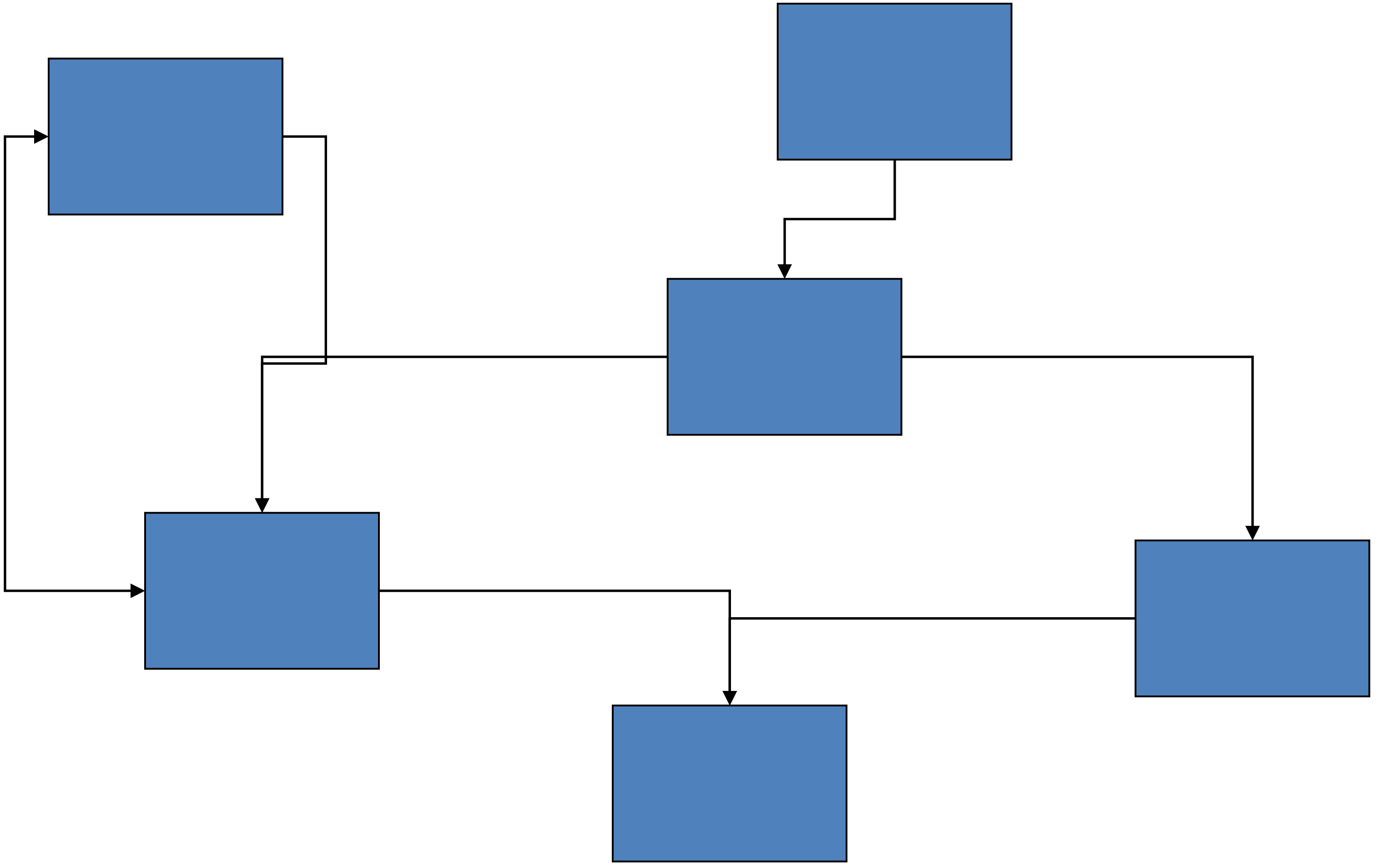
$$R_0 = S_0/\rho \quad \boxed{= 1.66}$$

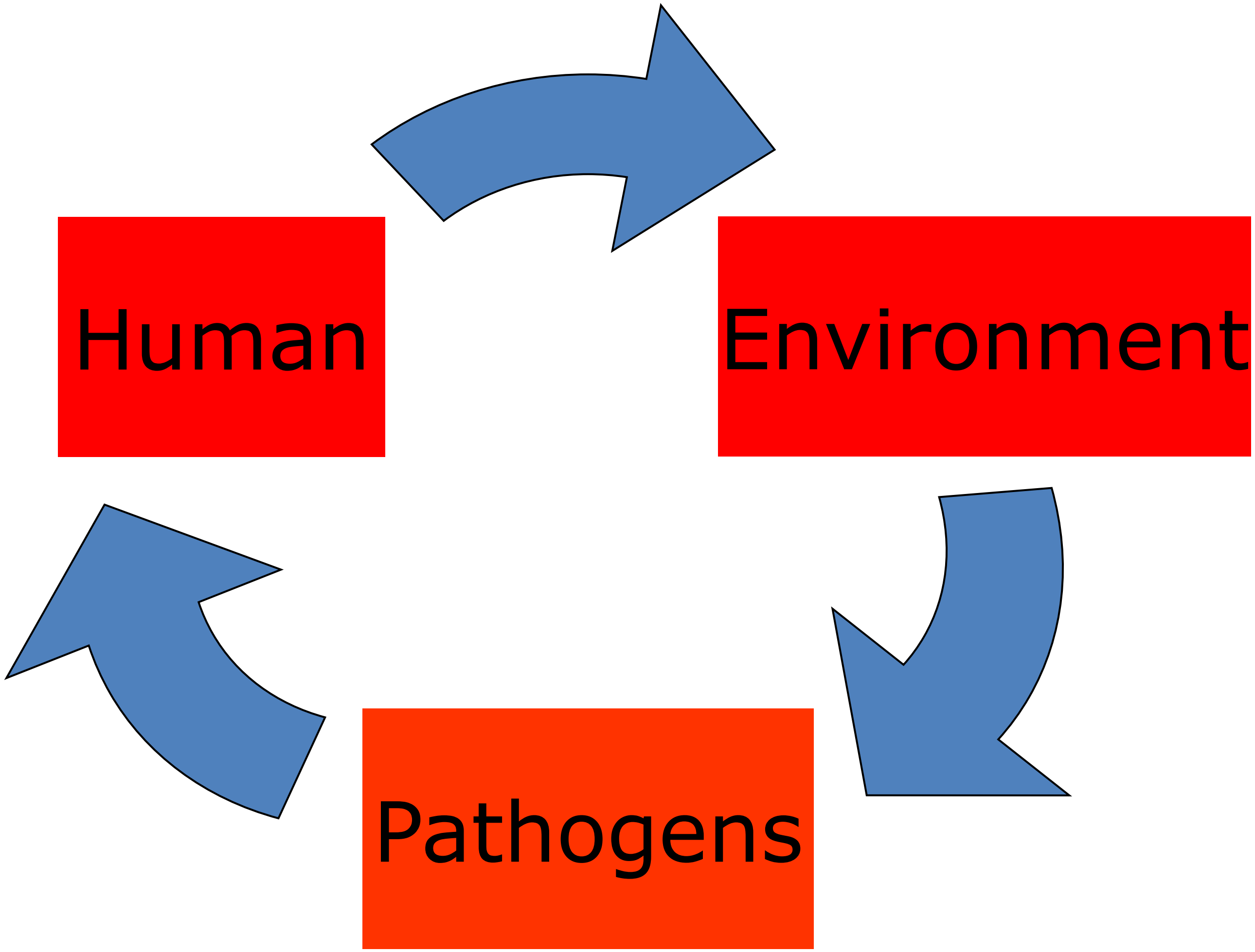
The records also show that the Infective period was **11 days (D)**

One can calculate, $\boldsymbol{\gamma = 1/D}$ $\boxed{= 1/11}$

$$\beta = \frac{\gamma}{\rho} = \frac{1}{11} \times \frac{1}{153} = 0.000594 \text{ (/ Day)} = 0.0178 \text{ (/ Month)}$$

General Framework




Human
Environment
Pathogens

Fundamental forms of compartment models

Models without vital dynamics

Models with vital dynamics

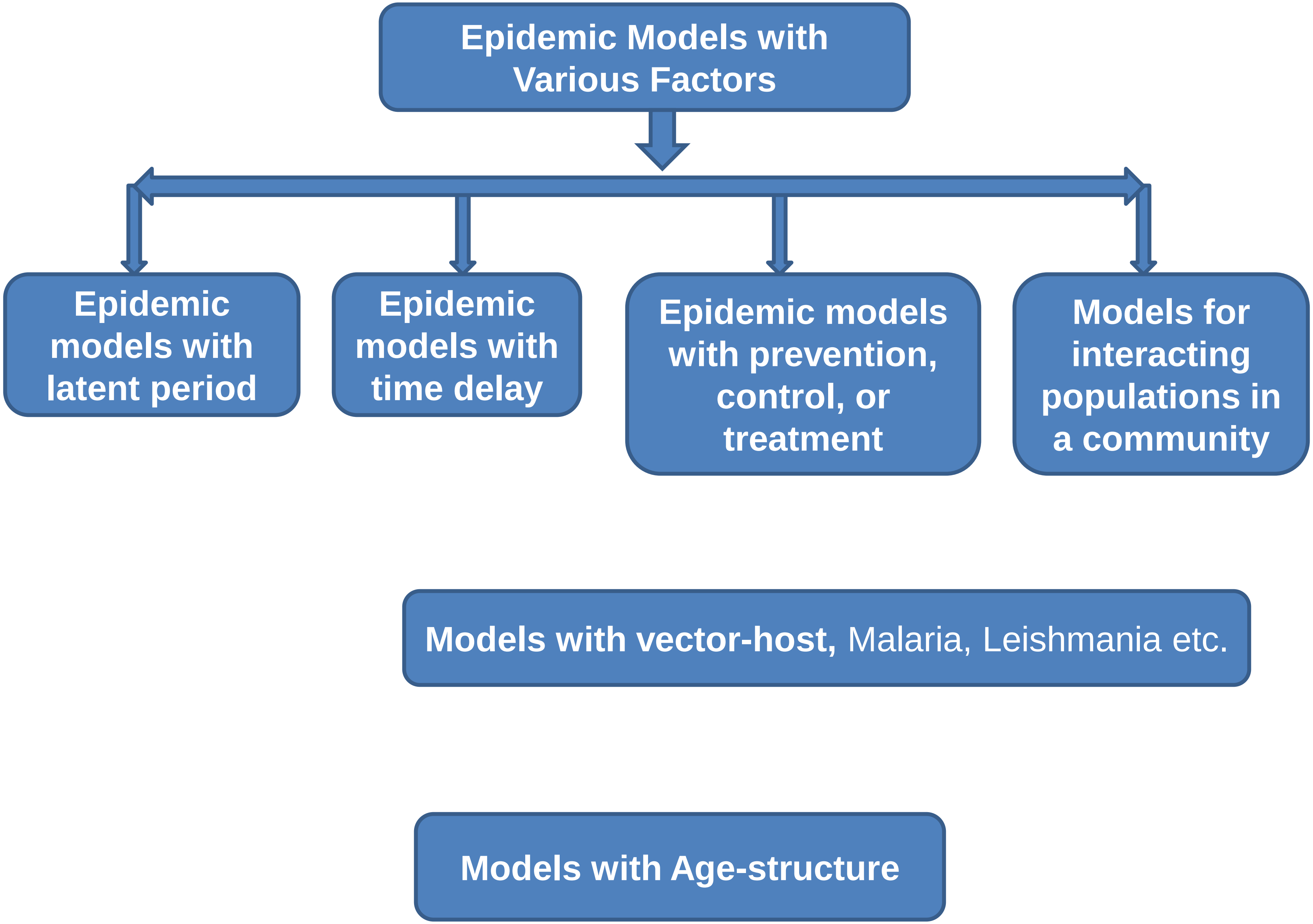
When a disease, such as **influenza, measles, rubella, or chickenpox**, spreads in a population rapidly, for a relatively short time, usually the vital dynamic factors, such as birth and natural death of the population, can be neglected in the models.

SIR *model* ***without vertical transmission***

In this model, we assume that the disease is not inherited from parents to their new generations, so that all the newborns are susceptible.

SIR model with vertical transmission

For many diseases, such as ***AIDS, hepatitis B, and hepatitis C,*** *newborns from the infected individuals can be infected as well. Such transmission is called vertical transmission.*


Epidemic Models with Various Factors
Epidemic models with latent period
Epidemic models with time delay
Epidemic models with prevention, control, or treatment
Models for interacting populations in a community
Models with vector-host, Malaria, Leishmania etc.
Models with Age-structure

Models with Vector-Host

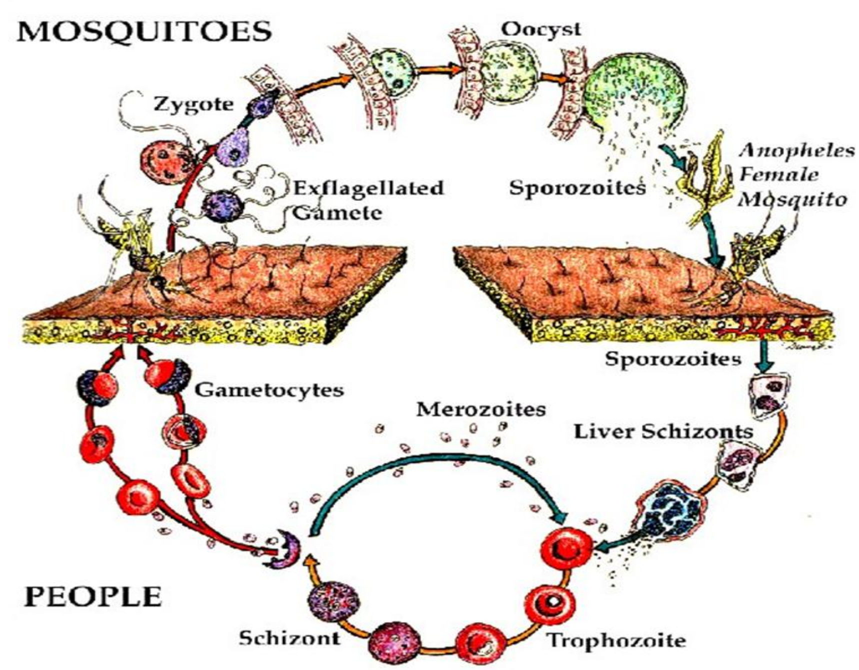
Ross Model on Malaria

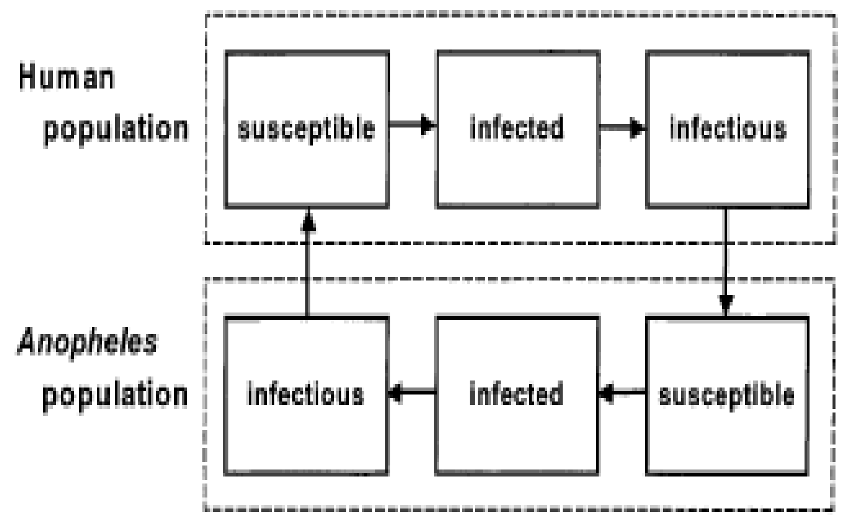
$$\frac{dx}{dt} = \sigma y\,(1-x) - \gamma x$$

$$\frac{dy}{dt} = acx\,(1-y) - \mu y$$

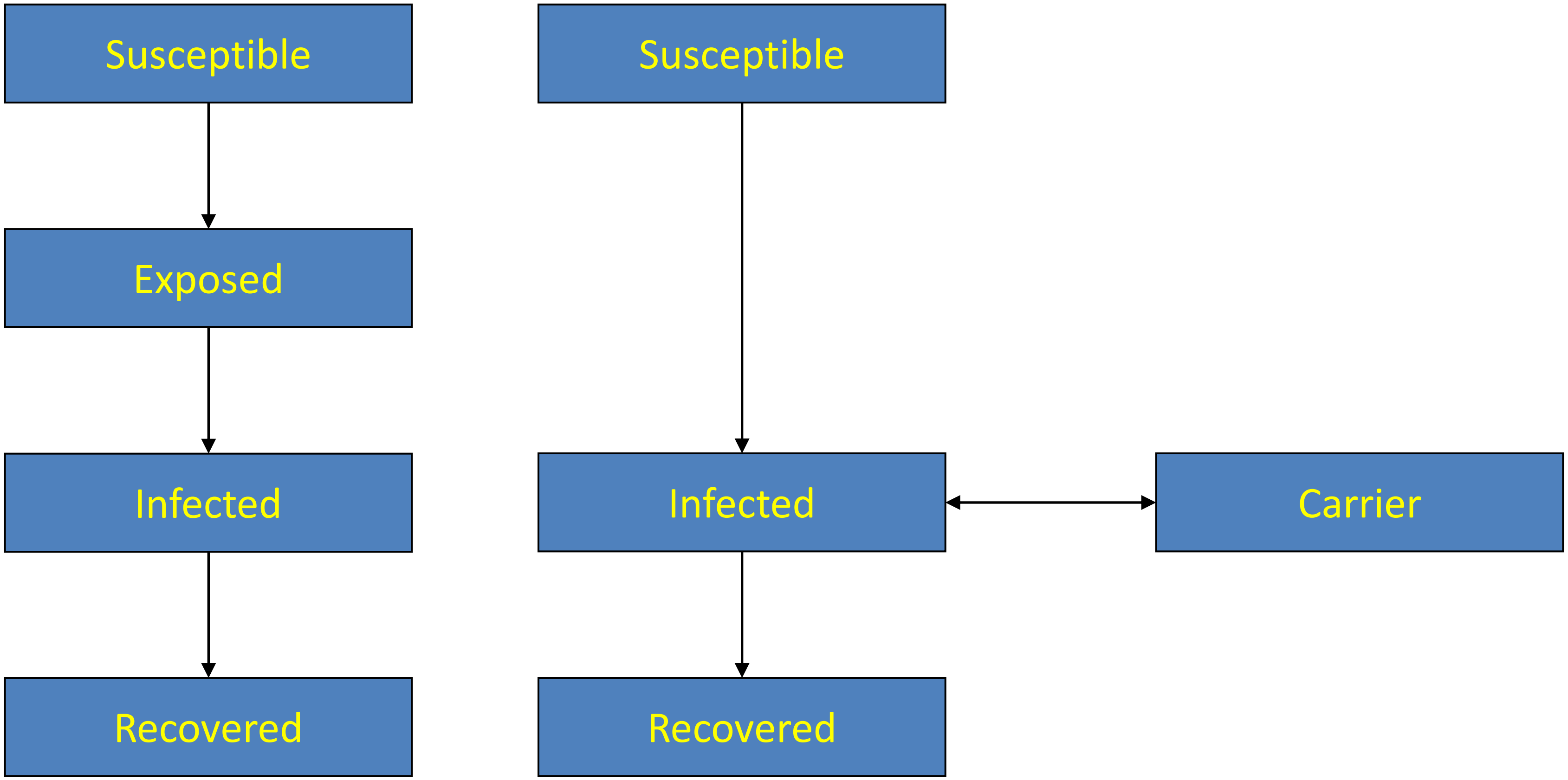
x: proportions of the infected human populations,
y: proportions of the infected female mosquito populations

a: bite rate of a single mosquito;
c: prop. of bites by suscpt. mosq. on inf. people that produce a patent infection;
γ: individual recovery rate per human;
μ: ind.death rate for mosq.;
σ = abM/N, N & M are the (constant) sizes of the human and female mosq. poplns. resp.;
b: prop. of inf. bites that produce an infection;



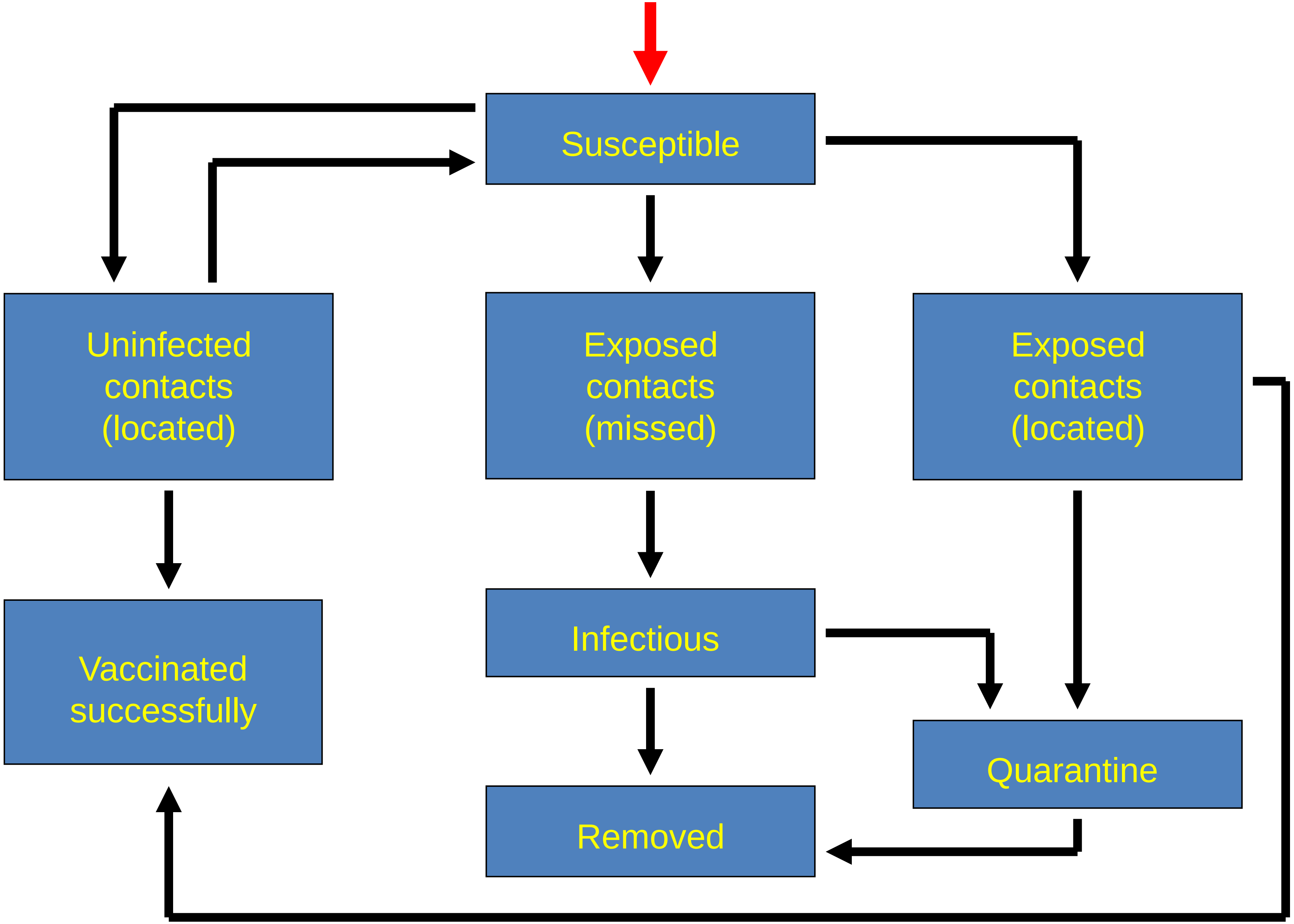


Modifications are (almost) endless



SEIR

Carrier Type Diseases: TB, Typhoid



Legrand et al. 2004, Epidemiol Infect, vol 132, pp19-25

Mathematical Models are applied to real situations to gain an understanding of medical and health issues

Examples:

Scientists are developing computer models to combat infectious diseases such as spread of **H5N1 strain of the avian influenza virus**.

Scientists are studying global warming through the use of computer models to simulate temperatures and rainfall in order to predict **environmental-based health risks such as cardiac and respiratory problems**.

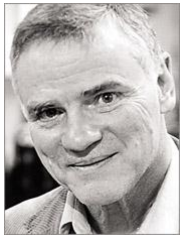
Teams of physical chemists have been using computer models to study brain that could help to understand **Alzheimer's disease.**

Kind of outcomes from models

- **Prediction of future incidence/prevalence under different vaccination strategies/"scenarios":**
  - age at vaccination,
  - population
  - vaccine characteristics
  - …
- **Estimate of the minimal vaccination coverage / vaccine efficacy needed to eliminate disease in a population**
- …

Also……there are application of mathematics to combat diseases at Molecular, Cellular and Tissue/Organ levels

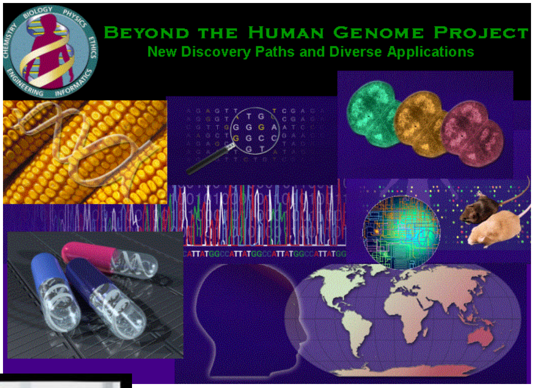
Major events in the history of Molecular Biology



Leroy Hood

1986 - 1995

- **1986** Leroy Hood: Developed automated sequencing mechanism
- **1986** Human Genome Initiative announced



1995-1996

- **1995** John Craig Venter: First **bactierial genomes** sequenced
- **1996** First eukaryotic genome-yeast-sequenced

1997 -

- **1997** E. Coli sequenced
- **1998** Complete sequence of the ***C.elegans*** genome
- **1999** First human chromosome (number 22) sequenced
- **2001** International **Human Genome Sequencing**: first draft
- **April 2003** Human Genome Project Completed. **Mouse genome** sequenced.
- **April 2004** Rat genome sequenced.

John Craig Venter

What are some Limitations of Mathematical Models

- Not necessarily a ‘correct’ model
- Unrealistic models may fit data very well leading to erroneous conclusions
- Simple models are easy to manage, but complexity is often required
- Realistic simulations are difficult and require more time to obtain parameters

Disclaimer

- **Models are not explanations and can never alone provide a complete solution to a biological problem.**

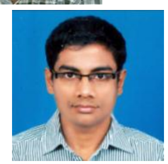
What We do……………………………

Our Team

Saikat Chowdhury (JRF)
[Physics; Bioinformatics]

Vidhi Singh (Project Fellow)
[Mathematics; Computer Sc.]

Abhishek Subramanian (JRF)
[Zoology, Bioinformatics]



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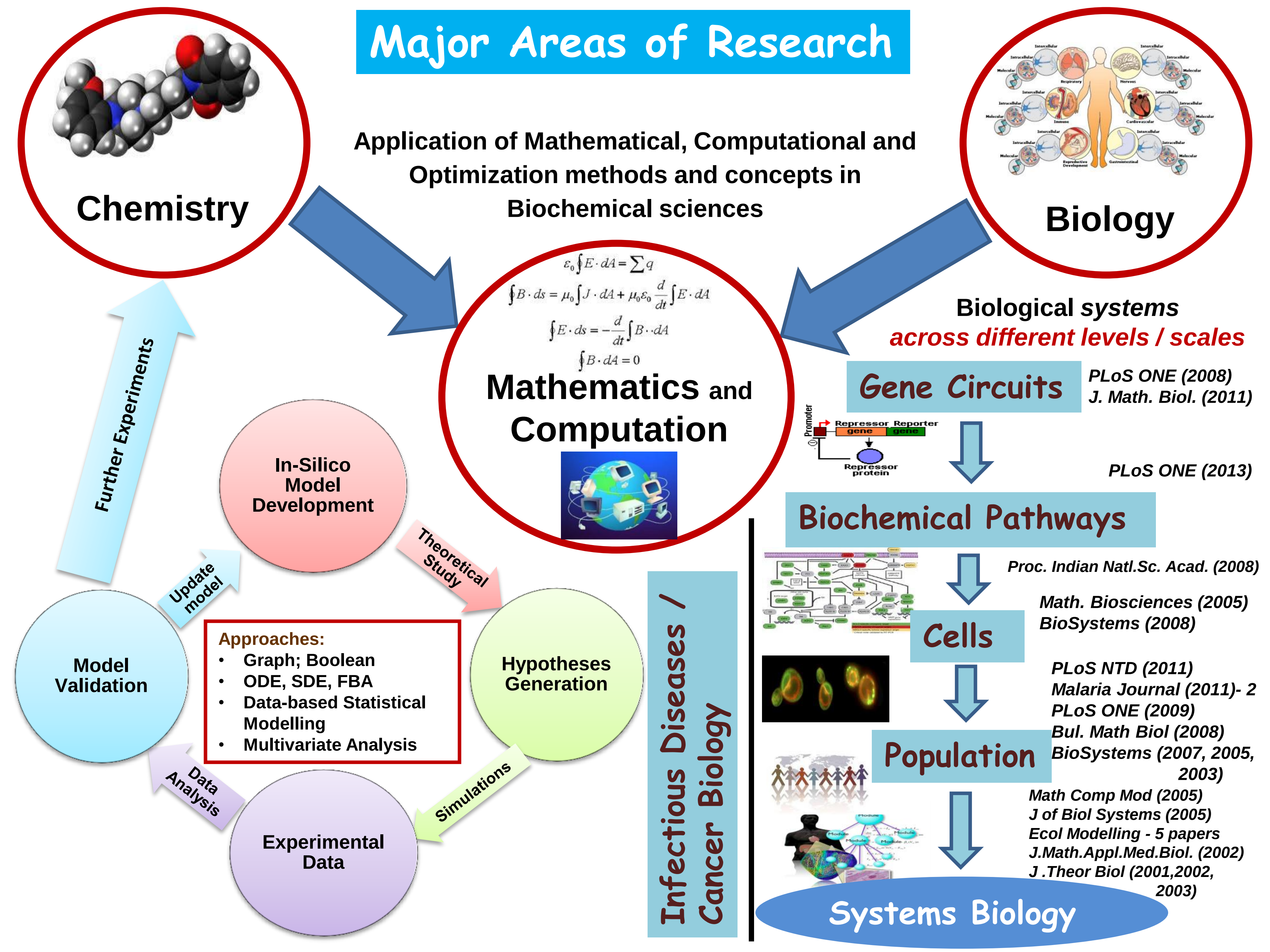
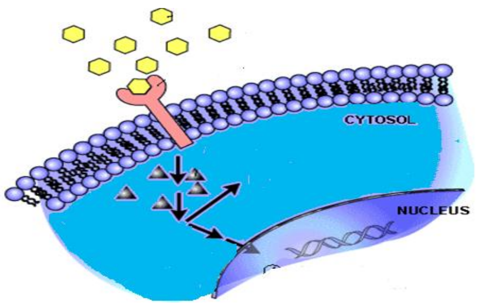
Piyali Ganguli (Project Assisstant)
[Bioinformatics and Biophysics]

Sutanu Nandi (JRF)
[Computer Sc.]

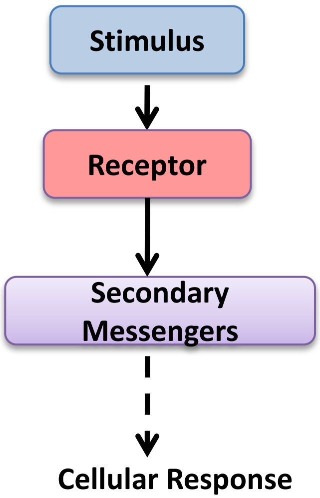


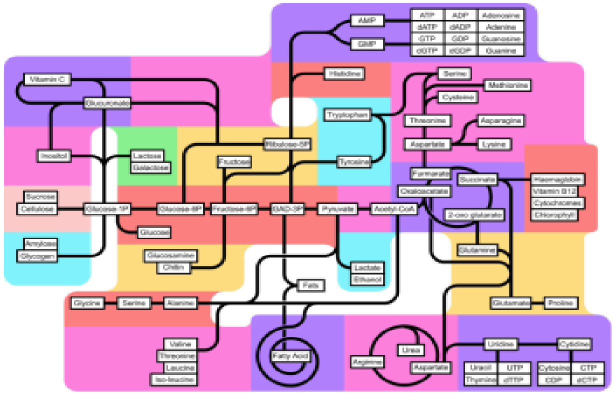
Major Areas of Research
Chemistry
Application of Mathematical, Computational and Optimization methods and concepts in Biochemical sciences
Biology
$\varepsilon_0 \oint E \cdot dA = \sum q$
$\oint B \cdot ds = \mu_0 \int J \cdot dA + \mu_0 \varepsilon_0 \frac{d}{dt} \int E \cdot dA$
$\oint E \cdot ds = -\frac{d}{dt} \int B \cdot dA$
$\oint B \cdot dA = 0$
Mathematics and Computation
Biological systems
across different levels / scales
Gene Circuits
PLoS ONE (2008)
J. Math. Biol. (2011)
Promoter
Repressor gene
Reporter gene
Repressor protein
PLoS ONE (2013)
Biochemical Pathways
Proc. Indian Natl.Sc. Acad. (2008)
Math. Biosciences (2005)
BioSystems (2008)
Cells
PLoS NTD (2011)
Malaria Journal (2011)- 2
PLoS ONE (2009)
Bul. Math Biol (2008)
BioSystems (2007, 2005, 2003)
Population
Math Comp Mod (2005)
J of Biol Systems (2005)
Ecol Modelling - 5 papers
J.Math.Appl.Med.Biol. (2002)
J .Theor Biol (2001,2002, 2003)
Systems Biology
Infectious Diseases / Cancer Biology
Further Experiments
In-Silico Model Development
Theoretical Study
Hypotheses Generation
Simulations
Experimental Data
Data Analysis
Model Validation
Update model
Approaches:
• Graph; Boolean
• ODE, SDE, FBA
• Data-based Statistical Modelling
• Multivariate Analysis

Intra cellular networks - Modeling of Intra-cellular Signaling and Metabolic Processes

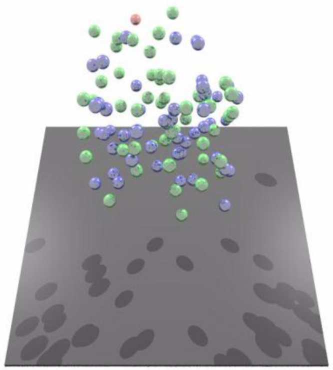


- Identification of potential drug targets, immuno-stimulators and easily targetable molecules
  - that can control Cancer cell progression

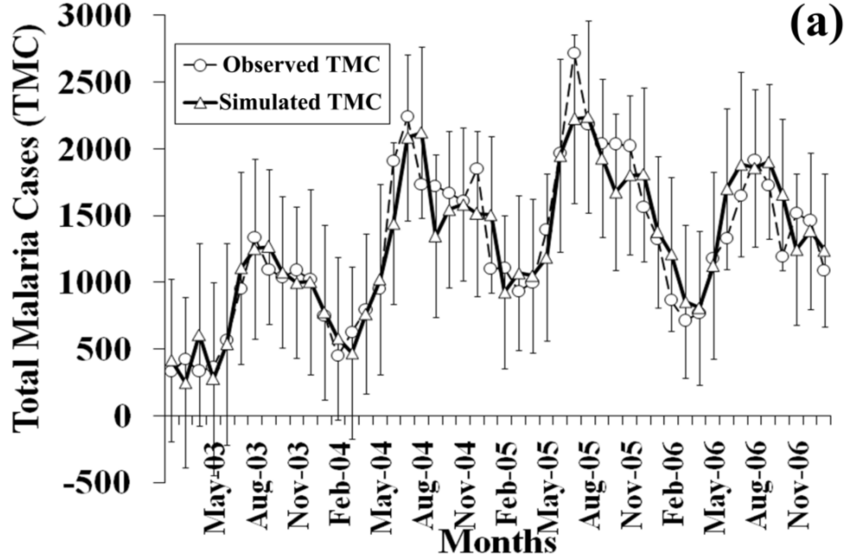




Study of Tumour Growth Pattern



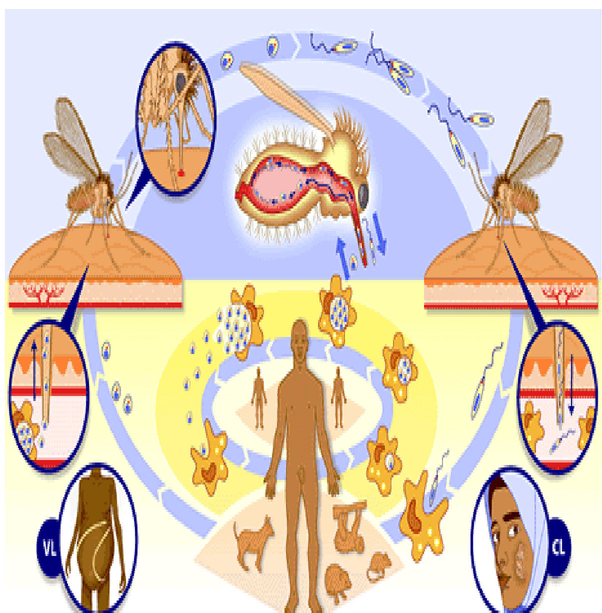
Mathematical Modelling and Forecasting of Malaria Incidence

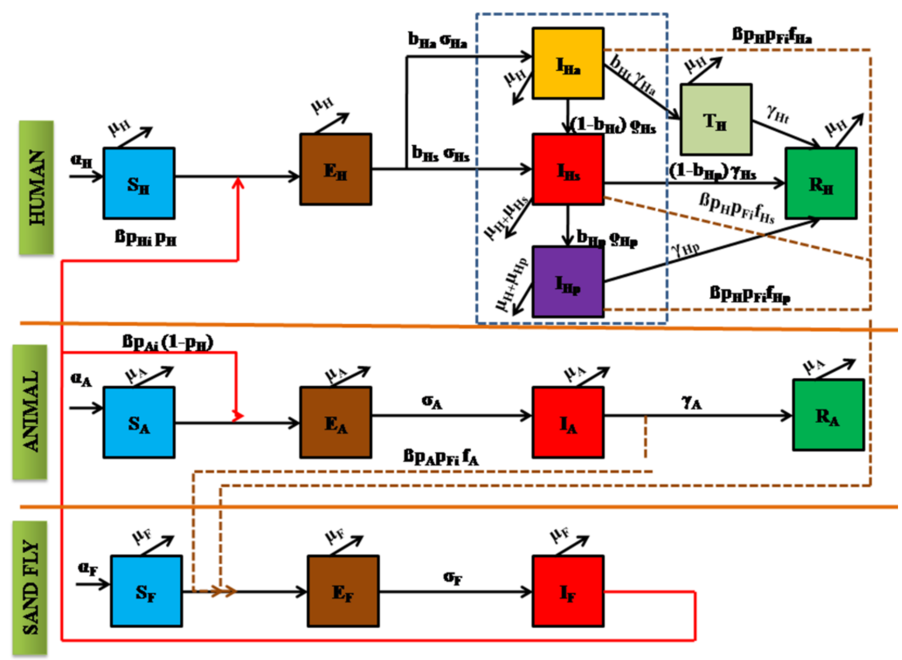


Effects of Rainfall, Temperature & Humidity

TMC = $6995.79 - 1087.87T + 4.03R - 1.44TMC_{-1} + 516.88(T_{-1}) + 40.03T^2 - 1.9\times10^{-4}R^2 - 2.1\times10^{-4}(TMC_{-1})^2 + 6.08(T_{-1})^2 + 5.68\times10^{-2}T\,R - 5.64\times10^{-2}\,TMC_{-1}T - 35.24TT_{-1} - 2.6\times10^{-04}\,TMC_{-1}\,R - 1.59\times10^{-1}R\,(T_{-1}) + 1.67\times10^{-1}TMC_{-1}\,T_{-1}.$

Mathematical Modelling and Forecasting of Leishmania Incidence (Kala-Azar)





Maths can be a real TRANSFORMER……
….Fighting against Diseases

Mosquitoes don't know maths…

So Human intervention is needed for control…

Acknowledgement

- Council for Scientific and Industrial Research (CSIR)
- Department of Biotechnology, Govt. of India
- Department of Science and Technology, Govt. of India

THANK YOU