

MATHEMATICAL MODELING

Methods and Application

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Mahidol University



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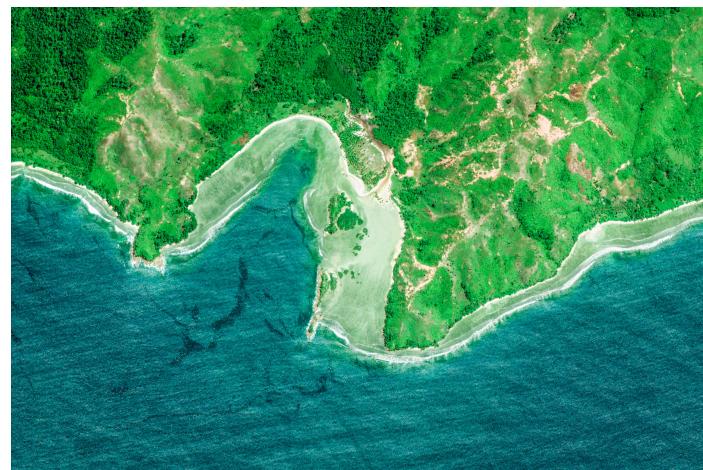
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DYNAMICAL SYSTEMS -

Modeling Techniques in Practice



Keywords:

epidemiology, systems biology, transmission,
networks, stochastic process, symbolic computation,
compartmental model, immunology,
biologically statistical data analysis, public health,
ecological systems, evolutionary dynamics,
health risk analysis

5.1 Fundamentals

5.1.1 Overview with Terms

A **dynamical system** is a mathematical object and a set of rules, which define how this object changes in time (evolution rules).

- The object can be anything, as long as it can be described by a set of numbers (hence the term *mathematical*), since only then we can compose the **mathematical equations** to describe **the evolution rules** for it.
- Sets of numbers, points, vectors, geometric figures, and such satisfy this criterion.

Two types of systems

- Discrete Dynamical Systems, and
- Continuous Dynamical Systems

Mathematical relevant techniques:

- Discrete → **difference equations** ("linear" vs "nonlinear", "single variable" vs "multivariate"),
- Continuous → **differential equations** ("ordinary" vs "partial"; "linear" vs "nonlinear").

Chapter learning objectives

Motivated by practical models, we will learn techniques to formulate the equations, to analyze their properties and solve found equations to find optimal or stable solutions.

Many good references on this subject include

- F.R. Giordano et. al.,
A First Course in Mathematical Modeling, 5th ed., **Cengage**, 2014.
- A Iserles, *A First Course in the Numerical Analysis of Differential Equations*, 2nd. **Cambridge University Press**, 2008
- Morris W. Hirsch, Stephen Smale, Robert L. Devaney, *Differential equations, Dynamical systems, and an Introduction to Chaos*, 3rd ed. **Elsevier**, 2013

Chapter blueprint- We will study in this chapter

1. Methods for Discrete Dynamical Systems (Section 5.2)
2. Continuous Dynamical System I- Single Species Growth in Section 5.3
3. Continuous Dynamical System II - ODEs for Species Interaction in 5.4
4. Continuous Dynamical System III- Epidemic models in Section 5.5
5. **Extra reading:** the Spread of a Contagious Disease (Section 5.7).

5.2 Methods for Discrete Dynamical Systems

Two key methods: (1) Method of Conjecture towards (2) System of difference equations

5.2.1 *Method of Conjecture in Discrete Dynamical Systems*

- STEPS
 1. Observe a pattern.
 2. Conjecture a form of the solution to the dynamical system.
 3. Test the conjecture by substitution.

4. Accept or reject the conjecture depending on whether it **does** or **does not** satisfy the system after the substitution and algebraic manipulation.

NOTE: For the conjecture to be accepted, the substitution must result in an identity.

- **Example:** Linear dynamical systems $a_{n+1} = r a_n$, for r constant.

Theorem 5.1

The solution of the linear dynamical system $a_{n+1} = r a_n$ (for any nonzero constant r), is

$$a_k = r^k a_0$$

where a_0 is a given initial value.



◆ EXAMPLE 5.1 (Sewage Treatment).

A sewage treatment plant processes raw sewage to produce **usable fertilizer and clean water by removing all other contaminants**. The process is such that

each hour 12% of remaining contaminants in a processing tank are removed.

Determine

1. What percentage of the sewage would remain after 1 day?
2. How long would it take to lower the amount of sewage by half?
3. How long until the level of sewage is down to 10% of the original level?

REQUEST: Build the model of the above process as a linear dynamical system.

GUIDANCE for solving.

Shall $r = 0.12$ be the hourly rate? Shall $a_{n+1} = r a_n$?

But what is a_n ?... How to find a_0 and determine the generic and explicit a_n ?

Concept of Equilibrium value- What and How?

Method of Conjecture needs few concepts as Equilibrium value...

- Consider a dynamical system of the form

$$a_{n+1} = r a_n + b,$$

where r and b are constants. What is **equilibrium value** or **fixed point**?

Definition 5.1 (Equilibrium value)

Fixed points are steady state solutions of dynamical system(s), or its difference equations.

A number c is called **fixed point** (an equilibrium value) of a dynamical system



$$a_{n+1} = f(a_n)$$

if $a_k = c$ for all $k = 1, 2, 3 \dots$ when $a_0 = c$.

Property of fixed points : Then $c = f(c)$. ■

Theorem 5.2

The equilibrium value a of a dynamical system $a_{n+1} = r a_n + b$ if $r \neq 1$ is

$$c = \frac{b}{1 - r}.$$

When $r = 1$ and $b = 0$ every number is an equilibrium value.

When $r = 1$ and $b \neq 0$ no equilibrium value exists.

**Theorem 5.3**

The **solutions** a_k of a dynamical system $a_{n+1} = r a_n + b$ are roots of the equation

$$a_k = d \cdot r^k + c, \quad (5.1)$$

for some constant d (that you must find out by using initial conditions)

where $r \neq 1$ and $c = \frac{b}{1 - r}$ is the equilibrium value.

**Question 1.**

Solve completely EXAMPLE 5.1 of Sewage Treatment process.

5.2.2 Method of Difference Equations

Key tools include - Systems of Difference Equations, can be used for the following problems.

- P 1: A Car Rental Company
- P 2: Discrete Epidemic Models

PROBLEM 5.1 (A Car Rental Company).

- A car rental service has distributorships in Hanoi and Saigon. The company specializes in catering to travel agents who want to arrange tourist activities in *both cities*.
- Consequently, some day a traveler will rent a car in one city and may either drop the car off in that city or in the second city at the end of day.
Travelers may begin their itinerary in either city.
- The company wants to determine *how much to charge* for this [drop-off convenience](#).

A Car Rental Company- Data

- The historical records reveal that 70% of the cars rented in Hanoi are returned to Hanoi, whereas 30% end up in Saigon.
- Of the cars rented from the Saigon office, 60% are returned to Saigon, whereas the remaining cars end up in Hanoi. Denote by

$$\begin{cases} H_n = \text{the number of cars in Hanoi at the end of day } n, \\ S_n = \text{the number of cars in Saigon at the end of day } n. \end{cases}$$

A Car Rental Company- Model

Our dynamical system possibly is represented by the following [system of difference equations](#)

- either

$$\begin{cases} H_{n+1} = 0.6 H_n + 0.65 S_n \\ S_{n+1} = 0.4 H_n + 0.35 S_n? \end{cases}$$

- or

$$\begin{cases} H_{n+1} = 0.7 H_n + 0.4 S_n \\ S_{n+1} = 0.3 H_n + 0.6 S_n \end{cases}$$

- The equilibrium values (H, S) for the system are those values of H_n and T_n for which **no change** in the system takes place.
- If the company owns 1400 cars then, **no matter how** many cars they distribute at the beginning day of its business, after several days the number of cars end up at Hanoi and Saigon are either $(H, S) = (600, 800)$ or $(H, S) = (800, 600)$



- PROBLEM 5.1 (A Car Rental Company) - done
- PROBLEM 5.2: Discrete Epidemic Models ?

In PROBLEM 5.2 we combine Difference Equations with Compartmental Models allowing us to quantify the transition or transmission rates among compartments.

*Difference Equations in Discrete Epidemic Modeling***PROBLEM 5.2 (Discrete Epidemic Models).**

Consider a disease that is spreading throughout the globe, as a new flu, SARS-CoV2.

The **Center for Disease Control and Prevention** is interested in knowing and experimenting with a model for this new disease before it actually becomes a real epidemic.

Let us consider the population divided into three categories:

susceptible, infected, and removed.

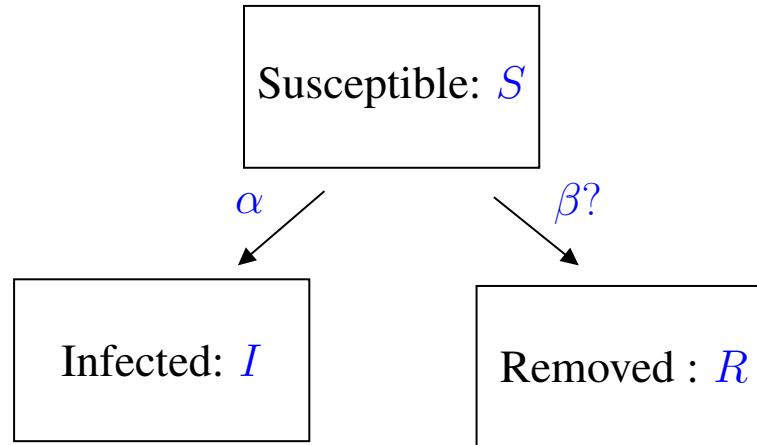
We make the following assumptions for our model:

- No one enters or leaves the community, and there is no contact outside the community.

- Each person is susceptible **S** (able to catch the flu);

infected **I** (currently has the flu and can spread the flu); or

removed **R** (already had the flu and will not get it again, which includes death).



- Initially, every person is either **S** or **I**.
- Once someone gets the flu this year, they cannot get the flu again.
- The average length of the disease is $5/3$ weeks, over which time the person is deemed infected and can spread the disease.

Our counts for the model will be per week.

Discrete Epidemic Model

- Basic compartment models (**SIR** models) in mathematical epidemiology are used to divide a population (or part/area of the population) into three subpopulations:

S (susceptible to) is suspected to be infected;

I (infected with) is infected; and

R (recovered, immunized or died)

Notation

$S(n)$ = number in the population susceptible after period n

$I(n)$ = number infected after period n (5.2)

$R(n)$ = number recovered/removed after period n .

In other words, **S**, **I** and **R** respectively describe sets of people suspected of being infected, being infected or recovered and became immune (or died) from a contagious disease infected in a total population of N individuals.¹

¹Details of infection progression are omitted, like *differences in individual responses to the virus*, but this is necessary when we firstly model the problem.

Discrete Epidemic Models - Model of $R(n)$

- The model we will consider is called the SIR model. Consider $R(n)$ firstly.
- Our assumption for the length of time someone has the flu is $mtf = 5/3$ weeks. Hence the removal rate is $r = 1/mrf = 3/5$. So 60% of the infected people will be removed each week:

$$R(n + 1) = R(n) + 0.6 I(n). \quad (5.3)$$

- The value 0.6 is called the **removal rate per week**.
- It represents the **proportion** of the infected persons who are **removed from infection each week**.

Discrete Epidemic Models - Model of $I(n)$

- Have terms that both increase and decrease its amount over time. It is **decreased** by the number of people removed each week: $0.6 * I(n)$.
- It is **increased** by the number of susceptible people who come **into contact with infected people**

and catch the disease: $a S(n) I(n)$.

- We define number a as the *rate at which the disease is spread, or the transmission coefficient*.

We realize this is a *probabilistic coefficient*.

- Assume initially that this rate is a constant value that can be found from the initial conditions.

$$I(0) = 5; \quad I(1) = I(0) - 0.6 * I(0) + a S(0) I(0)$$

In general

$$I(n + 1) = I(n) - r * I(n) + a S(n) I(n). \quad (5.4)$$

Discrete Epidemic Models - Model of $S(n)$

- Lets consider $S(n)$. This number is decreased only by the number that becomes infected.
- We may use the same rate a as before to obtain the model:

$$S(n + 1) = S(n) - a S(n) I(n). \quad (5.5)$$

- Conclude, our model now is

$$\begin{aligned} R(n+1) &= R(n) + r I(n) \\ I(n+1) &= I(n) - r * I(n) + a S(n) I(n) \\ S(n+1) &= S(n) - a S(n) I(n), \quad n = 0, 1, 2, 3 \dots \end{aligned} \tag{5.6}$$

What if we want to study the fatal pandemic in the real time scenario, that is allowing time point $n = t \in \mathbb{R}_+ = [0, +\infty)$? ■

HOMEWORK: Solve Problem 3: Actuarial science and personal financial matter (see CHAPTER 5 CONCLUSION in 5.6)



5.3 Continuous Dynamical System I-

Single Species Growth

Various natural phenomena give rise to mathematical models whose **system behaviors** are *time-dependent*, i.e., depend on time changes or rate changes. Those systems (and models) are represented by system of **differential equations** (DEs).

Definition 5.2

A differential equation is an equation that contains an unknown function and also involves derivatives of that function with respect to one or more independent variables.



- A differential equation that involves derivatives with respect to a single independent variable is an **ordinary** differential equation (ODE);
- A differential equation that involves derivatives with respect to more than one independent variable is a **partial** differential equation (PDE). ■

Example, $y'' + y' = e^x$ where $y = y(x)$ is a function of an independent variable x .

5.3.1 Modeling with differential equations

A specific class of ODE is First-Order Equations, having form

$$u'(t) = ku(t) \Leftrightarrow du/dt = ku$$

where $u(t)$ is an unknown function of time t , and k is a constant.

This ODE has solutions of the form $c \cdot \exp(kt) = ce^{kt}$.

This equation describes many different processes:

- * the growth of a population, the decay of radio nuclides,
- * the kinetics of simple chemical reactions, the **dynamics of certain populations.** _____

Growth of a population of Single Species via D. Equations

Basic concept that individuals divide to increase a population can be modeled mathematically using a differential equation, by Thomas Robert Malthus. Malthus² found small group of organisms obeyed growth law n 1798.

What is Exponential Growth?

Consider the classic example of bacteria on a petri dish. Let's say at hour n

- the number of bacteria x_n grows by 10% each hour and the initial population is $x_0 = 1000$.
- After the first hour: $x_1 = 1000 + (0.1) * 1000 = 1000 * (1.1)$

After the second hour: $x_2 = 1000 * (1.1) + (0.1) * (1000 * 1.1) = 1000 * (1.1) * (1.1) = 1000 * (1.1)^2$

After the third hour: $x_3 = 1000 * (1.1)^3$ etc.

- In general, $x_t = x_0(1 + r)^t$ which can be written as $x_t = x_0a^t$ where $a = (1 + r)$.

²a pioneer wrote *An Essay on the Principle of populations*. The book's essence is represented by the quasi-equation
a geometrically growing **population** + an arithmetically growing **food supply** = much **human misery**.
Malthus's book had tremendous influence on Charles Darwin and, in effect, provided him with the material basis for natural selection

SUMMARY -

The solution for the Bacteria is thus an exponential function of **base** $1 + r$.

The (discrete) dynamical system: $x_t = ax_{t-1}$ (**recurrent** relation/difference equation).

We just examined growth at some kind of finite increment using an average growth rate r over that increment. What happens if the **growth process is continuous**?

We get the model equation $x(t) = x_0 e^{rt}$?

HOW?

- Divide the growth process over the time increment into nt stages with the growth rate for each stage being $\frac{r}{n}$ where r is the average growth over the increment.

$$x(t) = x_0 \left(1 + \frac{r}{n}\right)^{nt}. \quad (5.7)$$

- Look at the limit as we divide our interval into ∞ pieces: $\lim_{n \rightarrow \infty} x_0[(1 + \frac{r}{n})^{n/r}]^{rt}$.
- We can pull x_0 out of the limit. In brackets we have the irrational number e :

$$x(t) = x_0 e^{rt}. \quad (5.8)$$

Exponential Growth: Solution properties

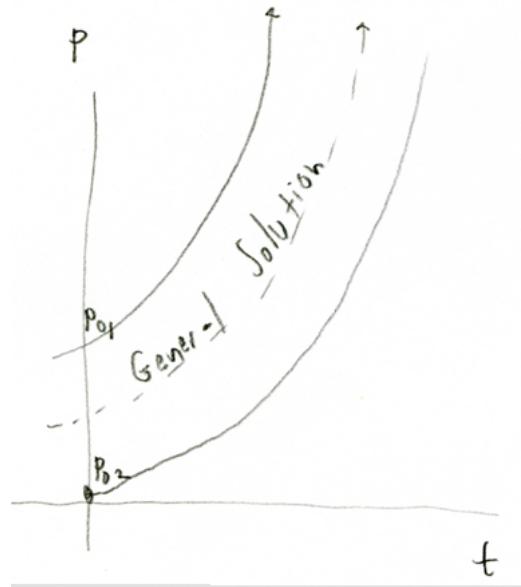
We can calculate the time to double the population (known as the "rule of 70" in financial circles)

$$t_{double} = \frac{\ln(2)}{r} \sim \frac{.70}{r}. \quad (5.9)$$

What does the solution look like? On a log plot, it is a straight line of slope r .

Is this realistic? **What if our growth rate was negative?**

- **Fact:** If $u'(t) = ku(t)$ has negative growth rate $k = -m < 0$, the no. bacteria x has



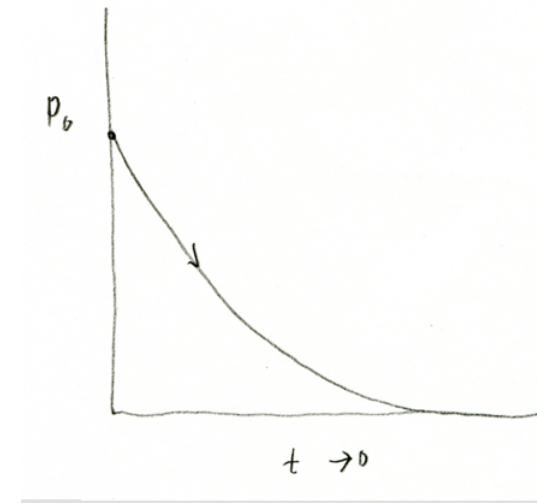
$$\dot{x} = -m x \quad (5.10)$$

- This shows exponential decay. Solution goes to zero, no matter what the *initial condition* was.

And most systems have both growth and decay terms.³

³

• Example, our phytoplankton equation [in Environment] will have terms for growth as a function of light, temperature, and nutrients, and decay (mortality).



5.3.2 Logistic growth - More realistic model: Finite Resources

- Known that growth **cannot** continue forever because of finite resources and in fact in simplified scenarios will reach a given constant level K , known as **the carrying capacity of the system**.
- Verhulst** (a pioneer) noticed that simple populations appear to be capped and added an additional term to remove excess capacity.

$$\dot{x} = rx\left(1 - \frac{x}{K}\right) \quad (5.11)$$

- We can always nondimensionalize this by the carrying capacity to give

$$\dot{x} = rx(1 - x) \quad (5.12)$$

This is commonly known as *logistic growth*.

Logistic Growth: Solution

- This equation has solutions that tend toward K for all initial conditions except for $x = x_o$ for which there is no growth (assuming there is no such thing as a negative population).
- So, this is mathematically equivalent to a density dependent growth rate $r' = r(1 - x)$.
- Solution to this equation is

$$x(t) = \frac{x_o K}{x_o + (K - x_o)e^{-rt}} \quad (5.13)$$

Arbitrary Growth: Polynomial, are of the general form

$$\dot{x} = g(x) \quad (5.14)$$

where $g(x)$ is a polynomial, $g(x) = a_o + a_1x + a_2x^2\dots$

$$g(x) = a_o + a_1x + a_2x^2\dots$$

- Malthus, all coefficients are zero except for $a_1 = r$. Growth rate constant
- Verhults (logistic), growth rate decreases monotonically
- $a_0 = 0$ by argument that a population can't spontaneously exist

- One can fit any population, but will not elucidate any dynamics

5.3.3 Properties of the systems

Critical Points (Fixed Points) - the case of Continuous Systems

Fixed points are **steady state solutions** of *ordinary* differential equations.

- For example, consider the general form of our single species population equation $\dot{x} = f(x)$:

$$\dot{x} = 0 \Rightarrow f(x) = 0 \quad (5.15)$$

- In ecosystem dynamics, these fixed points are also known as *critical points*. For the Malthus system (exponential growth), we have:

$$\dot{x} = \alpha x = 0 \Rightarrow \hat{x} = 0 \quad (5.16)$$

- There is only one critical point ($x = 0$). How could we reach this solution?

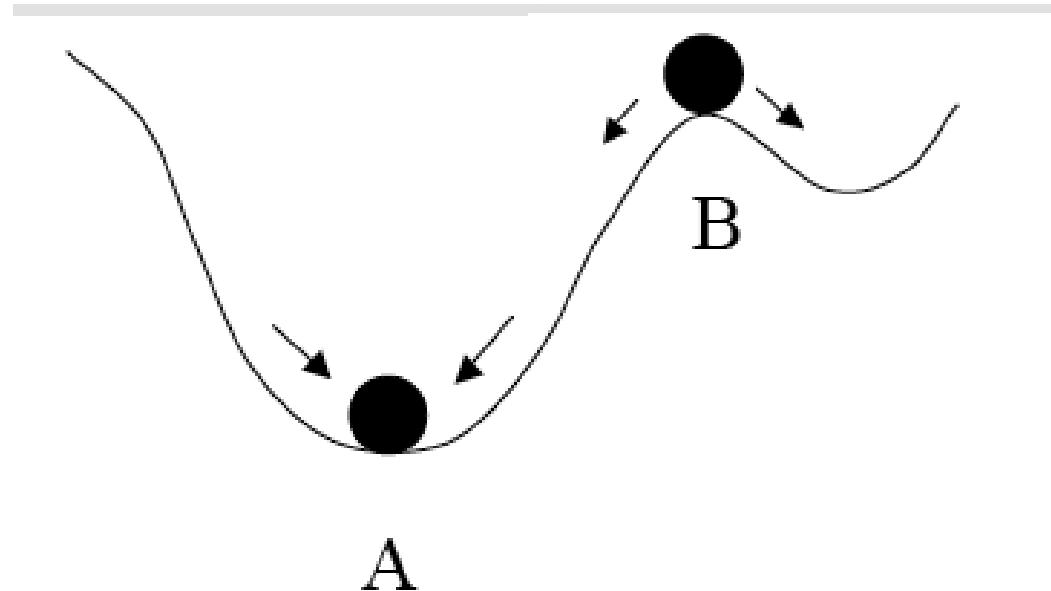
Stability of Critical Points

What is the nature of the solution near the critical point? Consider, two possibilities for a frog pond starting from a steady state:

1. Five frogs are killed in a freak accident. The frog population returns to the *stable* state.
2. The frog population crashes: *unstable*

- Let's look at the stability of our exponential growth $\dot{x} = \alpha x$ critical point $x = 0$.
- If we perturb x to $x = 5$, what will happen? $x(t) = x_0 e^{\alpha t} = 5e^{\alpha t}$.
- System will grow exponentially away from the critical point: *critical point is unstable*
- B: Unstable
- A: Stable

This example relates to states of **potential energy**, but the analogy holds for energy in an



ecosystem.

Stability of Critical Points: Logistic Equation

$$\dot{x} = \alpha x \left(1 - \frac{x}{K}\right) \quad (5.17)$$

Solve for fixed points with $\dot{x} = f(x) = 0$. Two fixed points:

1. $\hat{x}_1 = 0$ Nothing exists

2. $\hat{x}_2 = K$ Population is at carrying capacity

Through experiment: Are these stable?

1. $x = 0$: Perturb system from nothing, what will happen: *growth!* (Unstable)

2. $x = K$: Perturb system from carrying capacity, what will happen *return to K* (Stable).

We will analyze this - **Stability of Linear Systems** more rigorously.

FACT:

For linear ODEs of the form: $\dot{x} = \alpha x$, the stability can be determined simply from the sign of α :

- $\alpha > 0$: Unstable (growth)
- $\alpha < 0$: Stable (decay)

This is obvious from the solution: $x(t) = x_0 e^{\alpha t}$.

What about nonlinear ODEs? like the Logistic Equation?

$$\dot{x} = \alpha x \left(1 - \frac{x}{K}\right) ? \quad (5.18)$$

Trick is to *linearize about the critical point*.

What is linearization? We approximate a nonlinear function with a linear function that is quite accurate at a given point.

Linearization of nonlinear function $g(x)$

Using a Taylor Series near a given point for a nonlinear function $g(x)$.

- The following series $f(x)$ converges to the exact function $g(x)$ at $x = a$

$$f(x) = g(a) + g'(a)(x - a) + H.O.T. \quad (5.19)$$

- If we retain only the first two terms (zeroth order and linear) we have

the linearization $L(x)$ of the function $g(x)$ about the point a :

$$L(x) = g(a) + g'(a)(x - a) \sim g(x)$$

- What do we need to compute this linearization?
 1. The **first derivative** of the function $g(x)$ evaluated at the point $x = a$
 2. The value $g(a)$ of the function at point a

5.3.4 Stability of the Logistic Equation

- Let's analyze the stability of the critical points of the Logistic Equation.
- First, let's evaluate the first derivative:

$$f'(x) = \alpha - \frac{2\alpha x}{K} \quad (5.20)$$

- At the point $x = 0$, we have, for the Linearization:

$$L(x) = 0 + \alpha(x - 0) = \alpha x \quad (5.21)$$

- So, near the critical point $x = 0$, our logistic equation behaves as $L(x) = \alpha x$ (why is this **not** surprising). Thus it is an *unstable* critical point.
- At the point $x = K$, we have, for the Linearization:

$$L(x) = 0 - \frac{1}{2}\alpha(x - K) \quad (5.22)$$

- Thus, the linearized differential equation is:

$$\dot{x} \sim -\frac{1}{2}\alpha x + \frac{1}{2}K \quad (5.23)$$

- This is a stable differential equation with a single steady state value: $x = K$.
- So, the fixed point $x = K$ is stable.

This is **not** surprising, given an understanding of the solution $x(t)$ of the differential equation near $x = K$.

5.4 Continuous Dynamical System II -

ODEs for Species Interaction

Species Interaction- WHAT and HOW?

- We will now expand our analysis to more realistic system which include multiple, interacting

species. We study two fundamental models, the *predator-prey* and the *competing species*.

- Later, when we begin studying marine ecosystems, you should see the analogy with these fundamental models. For example, a classic NP model is a **predator-prey model where the nutrient is the prey and phytoplankton is the predator.**
- What do we hope to gain from the analysis:
 - What are the steady states of my system? Are my steady states stable or unstable?
 - How do the interaction parameterizations influence the system stability?
 - How does the system parameterization influence the dynamics of the system response (time scales, oscillation rates, relative magnitude of populations, etc)?

5.4.1 System of ODEs: Predator-Prey Models

We start with a fundamental model of species interaction : The *predator-prey* model.⁴

⁴HISTORY: Fur traders noted remarkable cycles in numbers of lynx and hare furs in the 1800s.

- Later, **Volterra** noted similar fluctuations in fish populations and derived a fundamental set of equations to describe them.
- Lotka** derived simultaneously a similar set of equations

Predator Prey (Lotka-Volterra) Equations

$$\frac{dx}{dt} = (ax - bxy) \quad (5.24)$$

$$\frac{dy}{dt} = (-cy + dxy) \quad (5.25)$$

Parameters:

- a: growth rate of prey; b: consumption of x by y
- c: natural mortality of y; d: consumption of x by y

Note: b and d are different because there is an efficiency to consumption. In this model, they were looking to answer few questions:

1. **Can we explain** the cycles in a typical predator-prey system?
2. **Why is it** that only in some systems the predation limits the prey density?
3. **What happens if** the state or parameters are changed?

For example, disease could alter the mortality rate, or a change in habitat could modify the ability

of the prey to hide and affect the rate of predation.

The model relates prey x and predator y and these variables

can represent biomass or population densities. Here we have used the following assumptions:

- There are *no time lags*, predators respond instantaneously to a change in the prey and vice versa
- Prey grow exponentially without predators to control their population. x
- Predators depend on prey to survive, otherwise, natural mortality will wipe them out c
- Predation rate depends on the likelihood that a predator comes across prey, thus is proportional to prey population - Growth rate of the predator is proportional to food intake...

5.4.2 System of ODEs: Consumption Responses

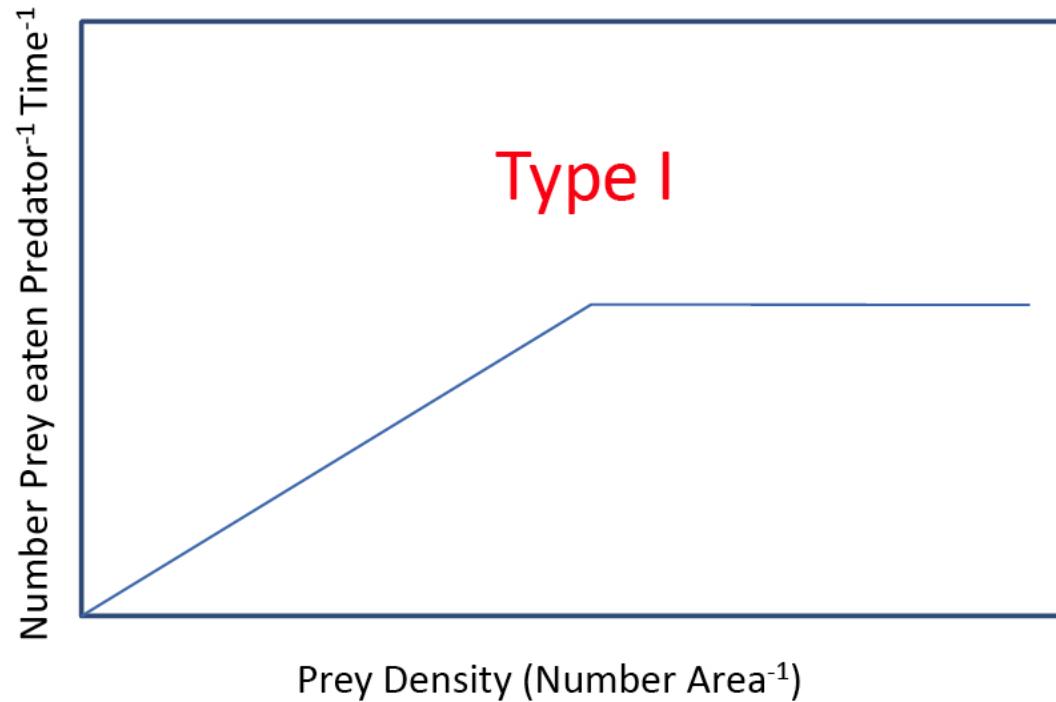


Figure 5.1: Type 1 Predation with Saturation (From UIdaho WLF 448)

- Is a linear dependence of predation rate on prey realistic?
- No, realistically, should consider additional ecosystem dynamics:

- *Saturation* Above a certain density of prey, the consumption will level out (can only eat so much).
- We will use this when we parameterize grazing of Z on P

Refuge : below a density, prey have places to hide:

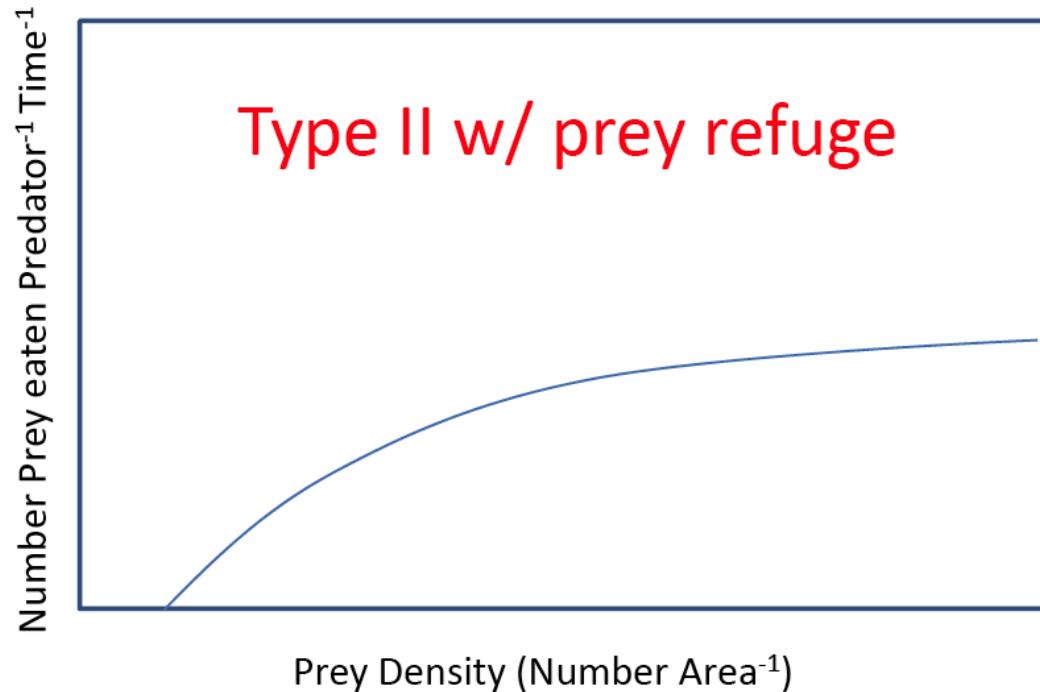


Figure 5.2: Type 2 Predation with Refuge Effects (From UIdaho WLF 448)

Nullclines (a.k.a. isoclines)

- **Nullcline:** Curve along which one of the variables is a steady state
- Along the x *isocline*, we have $f = 0$
- Along the x *isocline* the directional gradients must be parallel to the y -axis, but can be oriented up or down.

Analysis of L-V (Lotka-Volterra) model

1. Identify critical points in the system and think about their physical meaning
2. Plot the solution in phase (x,y) space using directional vectors
3. Examine Nullclines
4. Solve the full nonlinear system using Matlab and explore the results of phase plane trajectories by specifying a whole slew of initial conditions.

But first, we need to take a step backward and work on some quantitative tools.

First let's look at the generic representation of a coupled set of two ordinary differential equations,

the generic representation

$$\frac{dx}{dt} = f(x, y) \quad (5.26)$$

$$\frac{dy}{dt} = g(x, y) \quad (5.27)$$

Phase Space and Directional Gradients

Phase space is the space of state variables. If we plot, for example, the time-dependent solution of two state variables together, we are working in the *phase plane*.

Directional Gradients: Consider the governing equations in generic form:

$$\dot{x} = f(x, y) \quad (5.28)$$

$$\dot{y} = g(x, y) \quad (5.29)$$

We may not have an explicit solution for $x(t)$ or $y(t)$.

But we do have direct information on the rate of change of our two species.

For example, at the position in the phase plane x_1, y_1 , we have:

$$\dot{x}|_{x_1, y_1} = f(x_1, y_1) \quad (5.30)$$

$$\dot{y}|_{x_1, y_1} = g(x_1, y_1) \quad (5.31)$$

$$(5.32)$$

We may not know the solution $x(t), y(t)$, but the differential equations tell us at any point in the phase plane (x, y) what the rate of change of the solution with time is. We can approximate the derivative using a **forward Euler step**:

$$\dot{x} = \frac{dx}{dt} \sim \frac{x_1 - x_0}{t_1 - t_0} \sim f(x_0, y_0) \quad (5.33)$$

or given a solution (x_0, y_0) at t_0 , we can determine the approximate solution at t_1 :

$$\Delta x = x_2 - x_1 \sim (t_2 - t_1)f(x_1, y_1) \quad (5.34)$$

and

$$\Delta y = y_2 - y_1 \sim (t_2 - t_1)g(x_1, y_1) \quad (5.35)$$

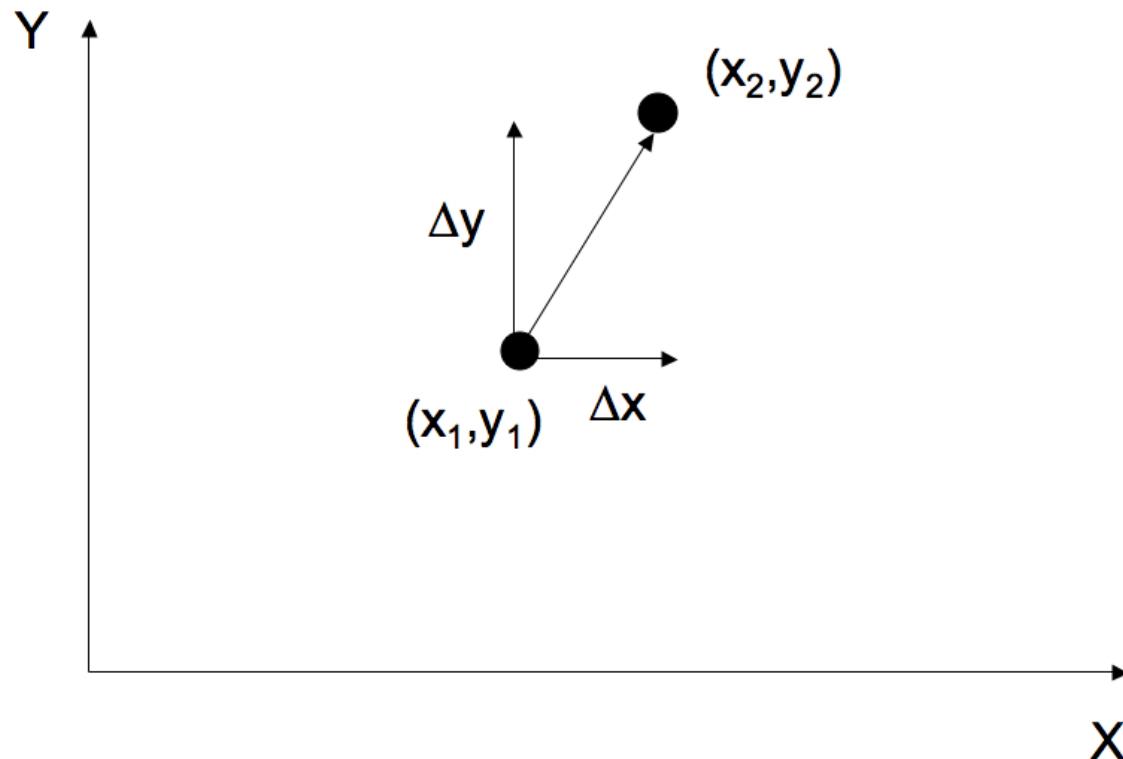


Figure 5.3: Phase plane, Model state moves from x_1, y_1 to x_2, y_2

So we can compute the vector at each point. If we only wish to piece together the gradients, then all we care about is the relative size of g and f and their signs.

FACT: We can normalize the vectors so they are all the same length (magnitude) but give different directions. If we evaluate the gradients at enough points, we can get a sense of the behavior of the system.

General procedure using Directional Gradients

The general procedure is as follows:

1. We plot our phase plane with species x on the x -axis and species y on the y -axis
2. We turn this into a regular grid of points, that is we divide up x into segments and y into segments so that we have a mesh of locations x, y . At each of these locations we evaluate our functions as above to find out what \dot{x}, \dot{y} are at each point.
3. We then draw an arrow with the tail located at the point x, y .

The head of the vector is located at the point $x + \delta x, y + \delta y$

where $\delta x = \frac{f(x,y)}{\sqrt{f^2+g^2}}$ and $\delta y = \frac{g(x,y)}{\sqrt{f^2+g^2}}$ relate to the rates of changes of prey x and predator y .

This arrow is pointing in the direction that ecosystem is going at the moment.

Nullclines (a.k.a. isoclines)- Reminder

- *Nullcline*: Curve along which one of the variables is a steady state
- Along the x *isocline*, we have $f = 0$
- Along the x *isocline* the directional gradients must be parallel to the y -axis, but can be oriented up or down

How do we determine the direction?

We look at the equation for \dot{y} and check the sign.

- If $\dot{y} = g(x, y) > 0$, y is increasing.
- We can also look at the y -nullcline along which $\dot{y} = 0$ and the directional gradients are parallel to the x -axis.

Work at Example: Pred-Prey

$$\frac{dx}{dt} = (ax - bxy) \quad (5.36)$$

$$\frac{dy}{dt} = (-cy + dxy) \quad (5.37)$$

Identify the critical points:

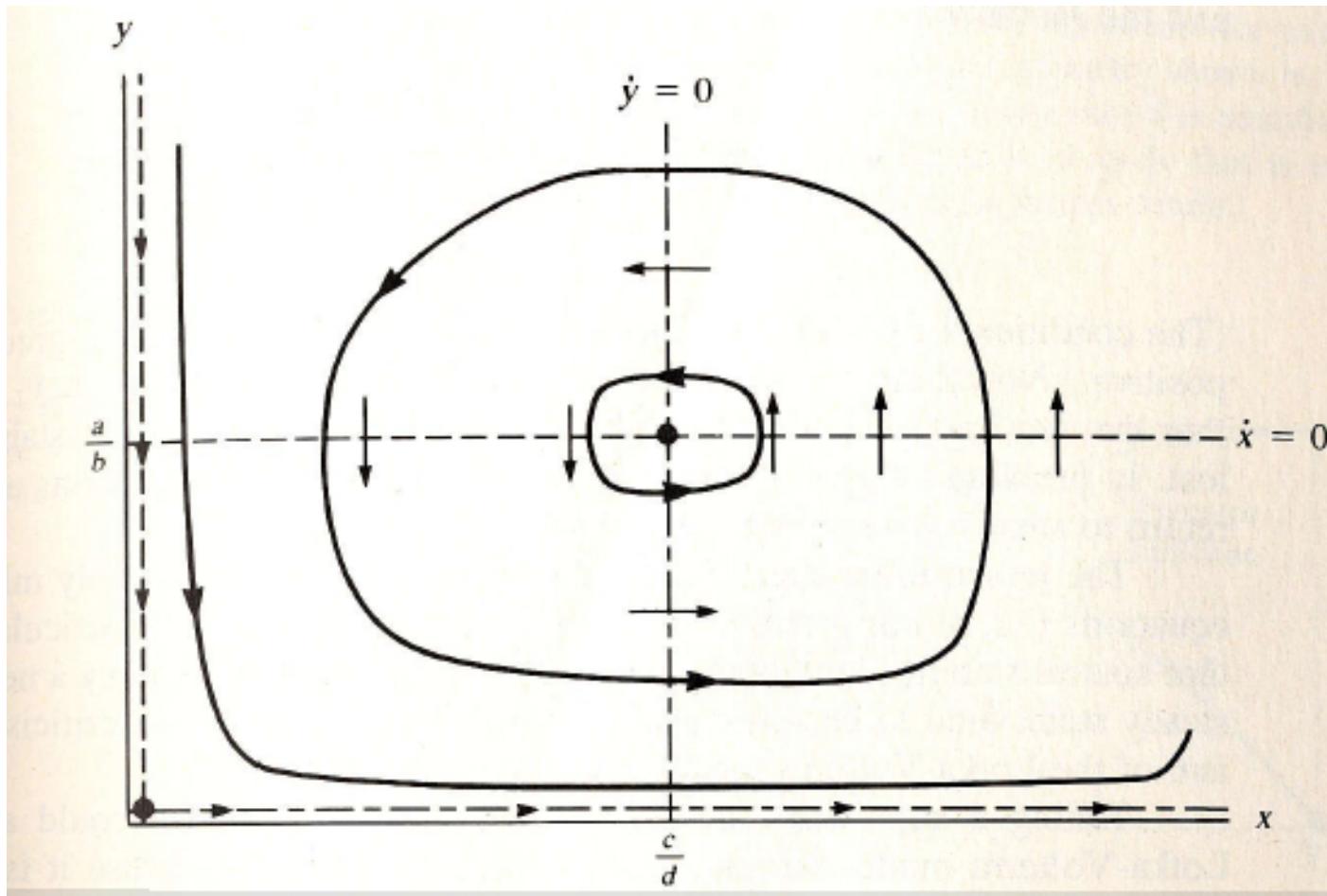
1. $\hat{x}_1, \hat{y}_1 = 0, 0$: Extinction of both species
2. $\hat{x}_2, \hat{y}_2 = \frac{c}{d}, \frac{a}{b}$: Growth equals mortality, clearly, the equations are coupled.

Nullclines of Pred-Prey

- **x nullcline** If we set $\dot{x} = 0$ we find that we have two straight lines, $y = \frac{a}{b}$ and $x = 0$. For this system, to the right of $x = \frac{c}{d}$ we have that $\dot{y} > 0$ and to the left we have that $\dot{y} < 0$.
- **y nullcline** If we set $\dot{y} = 0$ we find that we two straight lines given by $x = \frac{c}{d}$ and $y = 0$. Now, if we examine what happens to \dot{x} along the y nullcline, we see that when $y > \frac{a}{b}$, we have that $\dot{x} < 0$

and below that line, it is positive.

Sketch of pred-prey analysis



Q: What is happening in the ecosystem?

SUMMARY - Analysis of Critical Points

Summarized facts:

1. Where the nullclines intersect is, by definition, a critical point.
2. Every solution of the **predator-prey system** is a **closed orbit** (except the equilibrium point $Z = (c/d, a/b)$ and the coordinate axes).
3. In our **one-dimensional logistic equation** we were able to analyze the stability of the critical points by linearizing the system at the critical point.

Essentially, we transformed $\dot{x} = f(x) \Rightarrow \dot{x} \sim \alpha x$

For a coupled set of ODEs

$$\frac{dx}{dt} = f(x, y) \quad (5.38)$$

$$\frac{dy}{dt} = g(x, y) \quad (5.39)$$

The linear system is:

$$\dot{x} = a_{11}x + a_{12}y \quad (5.40)$$

$$\dot{y} = a_{21}x + a_{22}y \quad (5.41)$$

EPILOGUE - Solving nonlinear ODEs

- There are a few analytical techniques for solving nonlinear ODEs (e.g. separation of variables).
- However, for the complex form typical of dynamical systems, these do not generally work.

- We will have to use numerical techniques there (and Matlab will help greatly.)
- A well known solver we should review in detail is called *Runge-Kutta*.

Homework

- Do **ALL** exercises in both:

Section 1.4 (pages 52-56) **and** Section 11.1 (pages 468-470) in:

F.R. Giordano, W.P. Fox & S.B. Horton,

A First Course in Mathematical Modeling, 5th ed., Cengage, 2014.

- Next week plan: **Exercise Session**

5.5 Continuous Dynamical System III- Epidemic models

5.5.1 Standard Compartmental Model

Convention: $S = |\mathbf{S}|$, $I = |\mathbf{I}|$, $R = |\mathbf{R}|$ respectively are

the number of people suspected of being infected, infected and immunized, see more in

a recent paper [NVN2022]⁵ or see the next

Section 5.7 for a particular application domain where MM is a key.

- If $s(t) = S/N$ is the relative number of instances likely infected
and $j(t) = I/N$ is the relative number of instances already infected at time t ,

then the **dynamic progression of the infection process** is represented by

the 3-compartment system defined by the following (*deterministic SIR model*):

⁵NVN2022: Duc Q Nguyen, Nghia Q Vo, Thinh T Nguyen, Khuong Nguyen-An, Quang H Nguyen, Dang N Tran, and Tho T Quan. **Becaked: An explainable artificial intelligence model for covid-19 forecasting**. Scientific Reports, 12(1):1–26, 2022.

$$\begin{cases} \frac{ds}{dt} = -\alpha sj, \\ \frac{dj}{dt} = \alpha sj - \beta j \quad \text{and} \\ S \Rightarrow^\alpha I \Rightarrow^\beta R. \end{cases} \quad (5.42)$$

ELUCIDATION

1. The first two differential equations are a special case of the primitive model, expressed by the integral equations, first proposed by Kermack and McKendrick (1927) [Diekmann]. ⁶
2. The variation between compartments is depicted in the third diagram, meaning transition among sub-populations, $S \Rightarrow^\alpha I \Rightarrow^\beta R$.
 - The model parameter α is a constant indicating **infection rate**
(we assume that an individual infected with the virus is immediately infected, without integrating

⁶O. Diekmann Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Interpretation, **Mathematical and Computational Biology series**, (2000) Wiley book- 303 pp.

the incubation period-*latency*- into paradigm),

- β is a constant indicating **recovery rate** of an infected individual.

3. Relative number of recovered instances $r = R/N$ obtained by the law of conservation,

$$S + I + R = N \implies r(t) = 1 - j(t) - s(t),$$

t is the time variable.

4. Some of the most important quantities for quantifying infection are:

(i) **basic reproduction ratio** (*basic reproduction ratio*)

$$R_0 = \alpha/\beta$$

which is the average number of infected individuals (**level two**)

by an infected individual (**level one**) in the uninfected population

[technically *secondary infections per primary case in a ‘virgin’ population*];

(ii) **probability** $p(S, I, t)$ observed both the number of S potentially infected individuals and the number of I individuals was infected in the population N at a time t .

Property 5.1.

We see that the quantity R_0 plays a fundamental role in many different areas of biology but of the same evolutionary nature (e.g., on overcoming the therapeutic effects of cancer cells:

Meaning of basic birth rate

- (a) When $R_0 > 1$ and
- (b) the number of individuals potentially infected with s exceeds a threshold $s_c = 1/R_0$,
then an epidemic breaks out, because $ds/dt > 0$!

5.5.2 Spatial stochastic models

With given classes (population layers)

$$S(t) = \text{number in the population susceptible after time } t$$

$$I(t) = \text{number infected after time } t \quad (5.43)$$

$$R(t) = \text{number recovered/removed after time } t$$

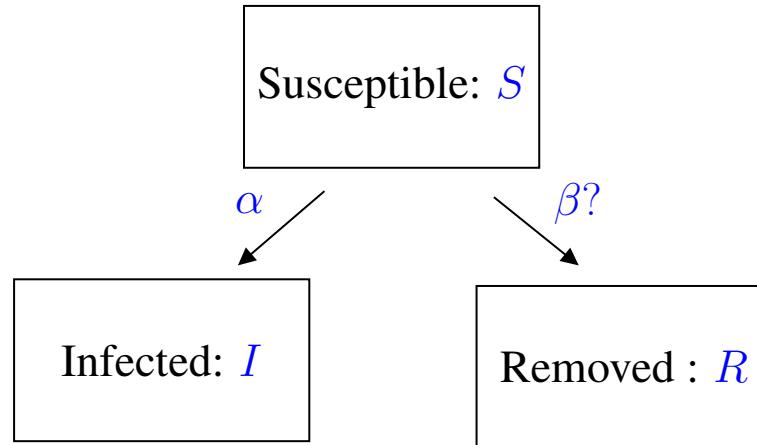
many extensions of the standard model (5.42)

$$\begin{cases} \frac{ds}{dt} = -\alpha s j, & \frac{dj}{dt} = \alpha s j - \beta j \quad \text{and} \\ S \Rightarrow^\alpha I \Rightarrow^\beta R. \end{cases} \quad (5.44)$$

have been proposed depending on the researcher's perspective and the goal of quantifying the parameters of interest. First, we can change the population structure by adding

class **L** (latent) containing individuals that are incubating the disease, or

class **T** (treatment) containing individuals being treated. . .



DISCUSSION 1.

Then we can examine the **SIS**, **SLIR** or **SIT** compartment models. We also allow for a more dynamic nature of infection, for example by adding a diagram stating that the interaction of a potentially infected individual with an infected individual gives two infected individuals at a rate α .

In paper [NVN2022]⁷ authors proposed the SIRD model (the final D stands for node Deceased / Death) in which we need four functions $S(t)$, $I(t)$, $R(t)$ and $D(t)$ and three model parameters

⁷Duc Q Nguyen, Nghia Q Vo, Thinh T Nguyen, Khuong Nguyen-An, Quang H Nguyen, Dang N Tran, and Tho T Quan. **Becaked: An explainable artificial intelligence model for covid-19 forecasting**. Scientific Reports, 12(1):1–26, 2022.

β , γ and μ to express the dynamic of a epidemic or pandemic. The model parameters β , γ and μ , however, timely depend on so many factors and abruptly change of huge data. The authors utilize **Deep Learning** approaches instead, and it well captured the COVID-19 data.

But the most important problem is how to put these models into computers, simulating what happens - under so high uncertainty of lots of factors in realtime scenarios- when the basic birth ratio R_0 is larger than one for a whole big population [say at least 100 million Vietnamese people (by 2023)]?



See next part for MODELING in Experimental Epidemiology where other approaches can be studied as well. ⁸ BRIEF REF. :

<https://www.bmjjournals.org/about-bmjj/resources-readers/publications/epidemiology-uninitiated/9-experimental-studies>

⁸Experimental epidemiology- the study of the relationships of various factors determining the frequency and distribution of diseases in a community.

5.6 CHAPTER CONCLUSION

SUMMARY- We studied in this chapter

1. Methods for Discrete Dynamical Systems (Section 5.2)
2. Continuous Dynamical System I- Single Species Growth in Section 5.3
3. Continuous Dynamical System II - ODEs for Species Interaction in 5.4
4. Continuous Dynamical System II- Epidemic models in Section 5.5

PROBLEM

PROBLEM 5.3 (Actuaries and personal financial matter). *with GUIDES*

Annuities are often planned for **retirement purposes**.

- **An annuity** is a saving account that pays interest on the amount present and allow the investor to withdraw a fixed amount each month until the account is depleted (i.e. completely consumed or used up).

- For now, consider 2% as the monthly interest rate and a monthly withdrawal of \$500.

This gives the dynamical system

$$a_{n+1} = 1.02 a_n - 500,$$

where the time unit n is month, and the money unit a_n is USD (\$).

- The equilibrium value for this dynamical system is 15000, 25000 or 30000 USD?

- FACT:

The solutions of a dynamical system $a_{n+1} = r a_n + b$, if $r \neq 1$, is

$$a_k = d \cdot r^k + \frac{b}{1 - r}. \quad (5.45)$$

- Assume that we completely consume (use up) the annuity in 5 years (or 60 months).

The value d in the solution a_k of our dynamical system $a_{n+1} = 1.02 a_n - 500$ is either $d = -9180.58$ or $d = -7619.55$? [see Equation 5.1].

PROBLEM 5.4.

Suppose the population on an isolated island is M . Suppose that there is currently an epidemic on this island that is spreading rapidly due to some of the island's residents traveling inland, immediately infected with the plague and brought the plague back to the island.

Let X be the number of infected residents on the island at time t

1. Let k be some suitable constant. Which of the following models is best suited to estimate X ?

A) $\frac{dX}{dt} = kX(X - M)$. B) $\frac{dX}{dt} = kX$.

C) $\frac{dX}{dt} = kX(M - X)$.

D) $\frac{dX}{dt} = kX(X + M)$.

2. The solution of the above suitable model will have the form

- A) $X(t) = \frac{X_0 M e^{-kt}}{X_0 + (M - X_0) e^{-kt}}$
- B) $X(t) = \frac{X_0 M}{X_0 + (M - X_0) e^{-kt}}$
- C) $X(t) = \frac{X_0 M}{X_0 + (M + X_0) e^{-kt}}$
- D) $X(t) = \frac{X_0 M}{X_0 + M e^{-kt}}$

3. Assuming the initial population on the island is $M = 5000$, on the second day ($t = 2$) after the epidemic there were 1887 people infected.

Predict the number of people infected on day 12 ($t = 12$) in this epidemic?

- E) $X(12) \approx 5000$. F) $X(12) \approx 4087$.
- G) $X(12) \approx 4945$.
- H) $X(12) \approx 4853$.

EXTRA READING SECTION

MODELING in Experimental Epidemiology



[Courtesy of Andre Derain]

Overview with A Systematic Approach

The structural complexity of **Epidemiology**, due to its involvement with many sciences such as microbiology, molecular biology, environment, mathematics, and sociology. . . today attracts the attention and cooperation of a multidisciplinary scientific community.

5.7 Experimental Epidemiology - A Mathematical Primer

We hence present in this section a short introduction to the subject of [Experimental Epidemiology](#) from the [Mathematical and Statistical Views](#), in fact just a small part of essential methods of **Mathematical- Statistical Modeling (MSM) in Epidemiology.**

Structural factors: The MM approach or experimental investigation of scientists and the corresponding practical actions of governments must consider a variety of factors such as:

1. In what locality (*geography*) has the infectious disease occurred?
2. What *genotype* does the microorganism have, has it been isolated or not (molecular biology)?
3. Are **population subgroups and preventive actions** for each group appropriate (sociological)?

Is the movement of individuals from one area to another (transportation) integrated into the mathematical model and **computer simulation?**

4. Are [agent-based numerical simulations on computers](#) possible and should we be concerned?

Studying the Spread of infectious diseases from the Computational Science perspective:

1. Modeling the reproduction and deformation of viruses

→ Modeling Shape-Shifting Viruses:

Part 5.3.1 will talk about the application of computational and simulation models in studying the evolution and shape changes of viruses, which are often thought to be the result of genetic mutations and often give rise to new, vicious strains of viruses.

2. Modeling the Immune System: focusing on human or animal subjects, is related to the basic mechanisms of pharmaceutical or vaccine preparation. [see in **Part 5.3.2** a description of the human immune system, and also a stochastic mathematical theory of microbial invasion (host) or escape (chemotherapy)].

3. Modeling the spread of disease across the population (Flu Spread), has recently developed a century, focusing on macro factors such as spread between segments of the population or regions within the country, between countries. → **Part 5.3.3** discusses the SIR theory.

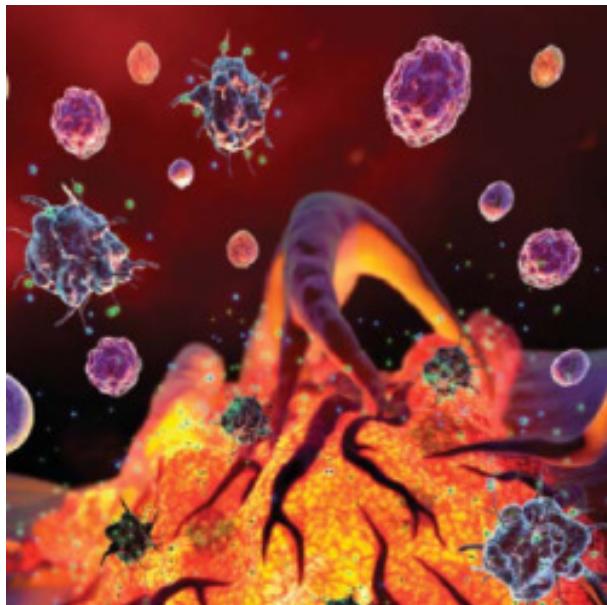


Figure 5.4: A typical virus -
Courtesy of Biomedical Computation 2017

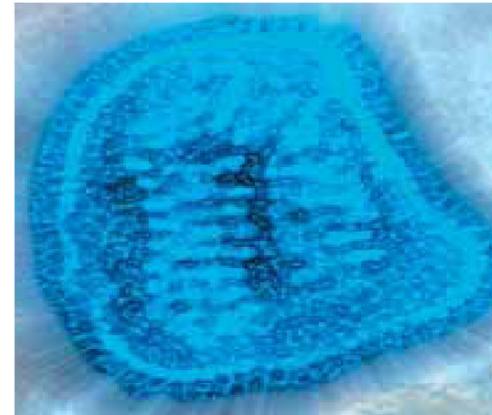


Figure 5.5: STMV Virus, the smallest virus (as in 2007)

5.7.1 Modeling virus reproduction and deformation

- **(I) Simulate viruses on computers at the molecular and atomic level**

The flu virus is an evolutionary marvel.

Every year many groups of experts try to design suitable influenza vaccines solely to deal with

the unusual reproductive abilities of these microorganisms, from genetic mutations of one strain or the combination of two different strains together. Few experts can predict when a virus strain that previously resided in *other animals* will mutate and successfully invade the **human immune system.**

- **(II) Predicting the strength of the virus (flu strain fitness)**

We need to model how the surface proteins of a flu virus strain (flu virus surface proteins) evolve, because, in influenza,

evolutionary fitness, i.e. the ability to survive and develop, is determined largely by the ability to invade the host immune system.

However, at the most microscopic level, there are a number of other related issues that need to be resolved with bioinformatics, before bringing the above simulation results into practice, as

a/ purifying virus genes (which produces weak viruses) or how to **avoiding**

b/ choosing more toxic or stronger sub-virus strains to design better and safer vaccines.

REF: Network Biology: Converging on Answers to Complex Diseases,
by Kristin Sainani, **Biomedical Computation**, www.bcr.org



5.7.2 *Modeling the immune system*

KEY: Using computational tools to understand influenza viruses and their structural proteins only shows part of the picture. It was **Charles Darwin** who said ‘It is not the strongest of the species that will survive, nor the most intelligent, but in fact it is those who respond fastest to changes in their surroundings’. In a hostile host immune system, the survival of the parasite depends not on its size or complexity, but on its adaptability.

Can invasion and escape be mathematically quantified?

According to genetic theory, when an organism wants to invade another individual or seek to

escape a hostile environment, some genetic mutations can be useful for the survival (sustainable replication) of that organism. Some common situations:

- (i) a parasite infects a new host,
 - (ii) cancer cells escape the effects of chemotherapy drugs,
 - (iii) viruses, bacteria or Microbes escape, ingest or become resistant to anti-microbial therapies
- seemingly unrelated, they actually have a common mathematical foundation, based on Darwin's evolutionary theory:

'An individual virus or parasite with a basic reproductive ratio less than 1 attempts to find better genetic mutations that will allow its descendants to survive'. [See **Property 5.1.**]

Iwasa- Michor- Nowak, three scientists at Harvard in 2004 ⁹ developed a mathematical theory that describes this evolutionary dynamics of invasion and escape.

- They describe a situation where a genetically heterogeneous population, due to survival, is

⁹Yoh Iwasa, Franziska Michor and Martin A. Nowak. Evolutionary Dynamics of Invasion and Escape, Journal of Theoretical Biology (2004); 226: 205-214

under pressure to invade another entity (environment, microbial strain or host) or must produce a generation of heroic descendants stronger and can resist an artificial hostile agent (vaccination, chemotherapy).

This mathematical theory is based on the **theory of multitype branching processes**.

- Although the research of the Iwasa-Michor-Nowak group provides an accurate analytical tool for studying evolutionary dynamics, there are [still some limitations in this model](#) when used in more complex processes.
- Those processes need mechanisms of mutation, and horizontal gene transfer- that is, between lineages - or express frequency-density dependent fitness while the basic assumption of the polytype branching process requires the independence of the lineages that provide and generate those mutations, see Franziska Michoret. al. ¹⁰

¹⁰Evolution of Resistance to Cancer Therapy, Current Pharmaceutical Design (2006), 12, 261-271 261.

Microarray technology and Statistics- hopeful views

Before 1995, scientists could only examine the activity of a few genes at the same time. Affymetrix, a microarray technology with a solid mathematical foundation (11) can be used to create Gene-Chips since 2000s. ¹² This is extremely important,

- i/ not only re-affirming the observations and experiences of clinical experimentalists,
- ii/ but rather it provides theoretical, mathematical evidence for isolating and following monitor a gene suspected of being involved in disease progression.

Although statistics develops more slowly than biology, after many problems related to microarray technology as mentioned above, fortunately statistical science is now changing to keep up with the needs of the life sciences! Under the pressure to find biologically meaningful results, many uniform solutions have been implemented: journals require authors to comply with many data-

¹¹based on the Latin square concept of combinatorial design theory, see T. Beth, D. Jungnickel and H. Lenz. Design Theory vol II, pp 880, Encyclopedia of Mathematics and Its Applications, Cambridge University Press (1999)

¹²Sorin Draghici Data Analysis Tools for DNA Microarrays, Mathematical Biology and Medicines Series, (2003) Chapman and Hall

related standards when publishing, for example

- (a) MIAME (Minimum Information About a Microarray Experiment), and
- (b) SAM and PAM (**Significance Analysis & Prediction Analysis of Microarrays**, or of any analysis of realistic human-being data) in the articles you want to publish.

Biologists have so realized the importance of collaborating with Computational scientists and Statisticians when researching, at least in exploiting *microarray technology*.

5.7.3 Spatial stochastic models

With given classes (population layers)

$$\begin{aligned} S(t) &= \text{number in the population susceptible after time } t \\ I(t) &= \text{number infected after time } t \\ R(t) &= \text{number recovered/removed after time } t \end{aligned} \tag{5.46}$$

many extensions of the standard model (5.42)

$$\begin{cases} \frac{ds}{dt} = -\alpha s j, & \frac{dj}{dt} = \alpha s j - \beta j \quad \text{and} \\ S \Rightarrow^\alpha I \Rightarrow^\beta R. \end{cases} \quad (5.47)$$

have been proposed depending on the researcher's perspective and the goal of quantifying the parameters of interest. First, we can change the population structure by adding class **L** (latent) containing individuals that are incubating the disease, or class **T** (treatment) containing individuals being treated. . .

Question 2 (Local, Regional to Global infection dynamics).

1. Looking at Vietnam, a medium size country, how do we know if the measures to quarantine a large population of a province in the Mekong Delta Region [when they would unfortunately be infected with a new *202x* Corona type] are actually strong?
2. Is it effective when a real epidemic has not yet broken out? We, of course, do not expect it to happen to draw conclusions!

3. Which model can express or track the fluctuations caused by individual-level spread of infection of the process when there are interactions between layers S_i , as well as between layers I_i , not to mention between layers S_i and layers I_j , when $1 \leq i \neq j \leq 64$?

Thus, the above concerns really have to be considered for at least two obvious reasons:

- (a) - large populations contain a multilayered structure, and
- (b) - the movement of individuals between levels (cities) are the potential for the spread of a large epidemic.

DISCUSSION 2.

- Interested in these issues from a modeling perspective, authors at the Max-Planck Institute (Germany) and the Institute of Theoretical Physics (UC Santa Barbara, USA), led by Professor Hufnagel, have proposed a probabilistic model to describe global disease transmission [13], including two levels:

¹³L. Hufnagel, D. Brockmann, and T. Geisel. Forecast and control of epidemics in a globalized world, PNAS (2004) Ecology series, 101; 15124-15129

dynamic local infection and
infection due to global travel and transactions of individuals.

- The Hufnagel group's model was validated using SARS data in Hong Kong (2003) provided by WHO and CDC (US): simulation results for 90 days (90 discrete points) showed agreement. quite perfect match between the event that happened and the simulated data.
- However, in Vietnam (or other poor countries), the most difficult point in learning, applying, improving this model or proposing a new model is **trustworthy experimental data** (especially for the health or traffic sectors, by 2021)!
- In principle, whether at the local, national or global level, a (properly validated) spatial models as **SIR** can be used to predict epidemiological endangered regions if the source of the outbreak is quickly and precisely located.

Question 3. *Most essential questions on spatial stochastic modeling are:*

1. Is vaccinating healthy people or isolating sick individual enough to prevent the spread of the disease?
2. If not, these measures must be coordinated, to what level should these measures be coordinated?

These questions have deep economic causes:

vaccinating a vast area or an entire population cannot afford the cost,

less number of vaccinated cases is unlikely to be effective, and in that case there must be alternative solutions to meet the needs of the population, to respond quickly to disease.

Isolating a village is okay, but a larger area is difficult, and if done,

the economic and commercial losses will be huge (negative impacts on economic growth) when

that area has financial or tourism significance (Saigon for example).

5.7.4 Algebraic- Computational- Stochastic approach

Readers interested in the relationship and impact of air transport on the spread of epidemics at the global level along with how to model that relationship can refer to articles ¹⁴.

A mathematical quantification of the effect of vaccination and isolation/quarantine measures on controlling or destroying the epidemic is very necessary. An algebraic-mathematical computational approach to biology might include views and actions:

1. **View:** an epidemic is considered a controllable dynamical system,
2. **Action:** find out whether there is a functional relationship between the action of isolation (input variables) and the vector including the number of individuals in the subclasses **I**(nfected) and **R**(ecovered) (output vector)?

¹⁴(A) Vittoria Colizza, Alain Barrat, Marc Barthélemy, and Alessandro Vespignani. The Modeling of Global Epidemics: Stochastic Dynamics and Predictability, Bulletin of Mathematical Biology (2006) 68:1893-1921.

(B) Matt J. Keeling and Ken T.D. Eames. Networks and Epidemic Models, Journal Royal Society Inter- face (2005); 2: 295-307

Using Algebraic- Computational- Stochastic method from both Theory and Simulation

- Cleverly combining matrix eigenvalue theory with Complex Analysis, such a functional relationship is established in 2005 by Chongli Jiang [¹⁵].

- What is more surprising is

the simulation by Hufnagel's group at the Max-Planck Institute (Germany) gave similar results to Jiang's theoretical work (in China).

Hufnagel's group, based on data from cities in North America and Europe, examined the relationship between

- (a) the probability $\text{Prob}(v)$ of needing to vaccinate a proportion v of the population and
- (b) the suppression of the epidemic when allow one infected individual A moving through regions $n = 1, 2$, or 3 times.

¹⁵Chongli Jiang, **Mathematical Mechanism of Quarantine Measures for SARS Epidemic**, The first International Conference on Algebraic Biology Japan (2005)

SUMMARY

In short, completely isolating outbreak points is more effective than cutting off some vital connections, at least according to the two studies mentioned above. However, in today's booming trade, like in Vietnam or Asia, it is worth examining how many feasible quarantine strategies are there? And then choosing the most effective and appropriate solution is very difficult, when you (the policymaker) insist on keeping the target of GDP growth higher than the previous year, or protecting the title of Ideal tourism, aimed at earning foreign currency, right?

Epilogue- A joint study, from the University of Washington - School of Public Health and Los Alamos Laboratory [¹⁶] reports a very large and detailed simulation of an epidemic scenario for the entire US population. In Vietnam, is it possible using only domestic resources to carry out, or at least prepare for, such (simulated) surveys, in order to predict the conclusions and necessary actions in the event of an epidemic outbreak? Are we not?

¹⁶Timothy C. Germann and al., Mitigation strategies for pandemic influenza in the United States PNAS (2006) Medical Sciences series, 103; 5935-5940

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Bibliography

- [1] ALEXANDER HOLMES, Introductory Business Statistics, OpenStax, Rice University, 2017
- [2] Annette J. Dobson and Adrian G. Barnett, *An Introduction to Generalized Linear Models*, Third Edition, CRC (2008)
- [3] Antal Kozak, Robert A. Kozak, Christina L. Staudhammer, Susan B. Watts *Introductory Probability and Statistics Applications for Forestry and Natural Sciences*, CAB (2008)
- [4] Canvas paintings by Australian artists of ethnic minorities, Australian National Museum
- [5] Esra Koca *Two-stage stochastic facility location problem with disruptions and restricted shortages* Journal of Computers & Industrial Engineering, vol 183, 2023 Elsevier.

- [6] John J. Borkowski's Home Page,
www.math.montana.edu/jobo/courses.html/
- [7] Warren B. Powell and Huseyin Topaloglu *Fleet Management, Applications of stochastic programming* / edited by Stein W. Wallace and William T. Ziemba, MPS-SIAM series on optimization (2005)
- [8] David S. Moore, George P. McCabe and Bruce A. Craig, 2009. *Introduction to the Practice of Statistics*, 6th edition, W. Freeman Company, New York
- [9] Man Nguyen, 2018. *Statistical Data Analysis I*, 1st edition, Mahidol University
- [10] S.R. Dalai and al., *Factor-covering designs for Testing Software*, *Technometrics* 40(3), 234-243, American Statistical Association and the American Society for Quality, 1998.
- [11] Douglas C. Montgomery, George C. Runger, *Applied Statistics and Probability for Engineers*, Sixth Edition, (2014) John Wiley & Sons
- [12] Jay L. Devore and Kenneth N. Berk,

- Modern Mathematical Statistics with Applications*, 2nd Edition, Springer (2012)
- [13] Johns Hopkins University, <https://www.jhu.edu/>
- [14] The U.S. Centers for Disease Control and Prevention, <https://www.cdc.gov/>
- [15] O. Diekmann *Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Interpretation*, Mathematical and Computational Biology series, (2000) Wiley book- 303 pp
- [16] George Streftaris and Gavin J Gibson. *Bayesian inference for stochastic epidemics in closed populations*, Statistical Modelling (2004); 4: 63–75
- [17] Matt J. Keeling and Ken T.D. Eames. *Networks and Epidemic Models*, Journal Royal Society Interface (2005); 2: 295-307
- [18] Yoh Iwasa, Franziska Michor and Martin A. Nowak. *Evolutionary Dynamics of Invasion and Escape*, Journal of Theoretical Biology (2004); 226: 205-214
- [19] Franziska Michor, Martin A. Nowak and Yoh Iwasa. *Evolution of Resistance to Cancer Therapy*, Current Pharmaceutical Design (2006), 12, 261-271 261
- [20] Sudhir Gupta. *Balanced Factorial Designs for cDNA Microarray Experiments*, Communications in Statistics: Theory and Methods, Volume 35, Number 8 (2006) , pp. 1469-1476
- [21] Sorin Draghici Data Analysis Tools for DNA Microarrays, Mathematical Biology and Medicines Series, (2003) Chapman and Hall book- pp
- [22] Niko Beerenwinkel and al. *Computational methods for the design of effective therapies against drug resistant HIV strains* Bioinformatics Review, Vol. 21 no. 21 (2005), 3943-3950
- [23] Niko Beerenwinkel *Evolution on Distributive lattices* Journal of Theoretical Biology Volume 242, Issue 2, 21 (September 2006), Pages 409-420
- [24] Lior Pachter and Bernd Sturmfels, editors, *Algebraic Statistics for Computational Biology*, Cambridge University Press (2005) book- pp

- [25] Zhang, Ma and Wu, *A compartmental model for analysis of SARS transmission patterns and outbreak control measures in China*, **Applied Mathematics and Computation**, 162, (2005)
- [26] Jorg Waldvogel *The Period in the Volterra-Lotka Predator-Prey Model* **SIAM Journal on Numerical Analysis**, Vol. 20, No. 6. (Dec., 1983), pp. 1264-1272.
- [27] Kristin Cobb. *Microarrays: The Search For Meaning in a Vast Sea of Data* **Biomedical Computation Review**, (Fall 2006) Special issues on Microarrays Technology
- [28] M. F. Fecko and al., *Combinatorial designs in Multiple faults localization for Battlefield networks*, **IEEE Military Communications Conf.**, Vienna, 2001.
- [29] Glonek G.F.V. and Solomon P.J. *Factorial and time course designs for cDNA microarray experiments*, **Biostatistics** 5, 89-111, 2004.
- [30] Hedayat, A. S., Sloane, N. J. A. and Stufken, J. *Orthogonal Arrays*, Springer-Verlag, 1999.
- [31] Robert V. Hogg, Joseph W. McKean, Allen T. Craig *Introduction to Mathematical Statistics*, Seventh Edition Pearson, 2013.
- [32] Paul Mac Berthouex, Linfield C. Brown, *Statistics for Environmental Engineers*, 2nd Edition, LEWIS PUBLISHERS, CRC Press, 2002
- [33] Michael Baron, *Probability and Statistics for Computer Scientists*, 2nd Edition (2014), CRC Press, Taylor & Francis Group
- [34] R. H. Myers, Douglas C. Montgomery and Christine M. Anderson-Cook *Response Surface Methodology : Process and Product Optimization Using Designed Experiments*, Wiley, 2009.
- [35] Man Nguyen, Tran Vinh Tan and Phan Phuc Doan, *Statistical Clustering and Time Series Analysis for Bridge Monitoring Data*, Recent Progress in Data Engineering and Internet Technology, Lecture Notes in Electrical Engineering 156, (2013) pp. 61 - 72, Springer-Verlag

- [36] Man Nguyen and Le Ba Trong Khang. Univ. Press, 2005
Maximum Likelihood For Some Stock Price Models, Journal of Science and Technology, Vol. 51, no. 4B, (2013) pp. 70- 81, VAST, Vietnam
- [37] Nguyen Van Minh Man, [41] Paul Mac Berthouex. L. C. Brown. *Statistics for Environmental Engineers*; 2nd edition (2002), CRC Press
Computer-Algebraic Methods for the Construction of Designs of Experiments, Ph.D. thesis
- [42] Ron S. Kenett, Shelemyahu Zacks.
Modern Industrial Statistics with applications in R, MINITAB, 2nd edition, (2014), Wiley
- [38] Nguyen, Man V. M. *Some New Constructions of strength 3 Orthogonal Arrays*,
the Memphis 2005 Design Conference Special Issue of the **Journal of Statistical Planning and Inference**, Vol 138, Issue 1 (Jan 2008) pp. 220-233.
- [43] Sheldon M. Ross. *Introduction to probability models*, 10th edition, (2010), Elsevier Inc.
- [44] Google Earth, Digital Globe, 2014- 2019
- [45] Vo Ngoc Thien An, Design of Experiment for Statistical Quality Control, Master thesis, LHU, Vietnam (2011)
- [39] Nathabandu T. Kottekoda, Renzo Rosso. *Applied Statistics for Civil and Environmental Engineers*, 2nd edition (2008), Blackwell Publishing Ltd and The McGraw-Hill Inc
- [46] Larry Wasserman, *All of Statistics- A Concise Course in Statistical Inference*, Springer, (2003)
- [40] Man Nguyen (2005) *Computer-algebraic Methods for the Construction of Design of Experiments*, Ph.D thesis, Eindhoven
- [47] C.F. Jeff Wu, Michael Hamada *Experiments: Planning, Analysis and Parameter Design Optimization*, Wiley, 2000.

- [48] Wendy L. Martinez and Angel R. Martinez, *Computational Statistics Handbook with MATLAB*, CHAPMAN & HALL/CRC, 2002
- [49] Sara M. Grundel et.al. *How to Coordinate Vaccination and Social Distancing to Mitigate SARS-CoV-2 Outbreaks?* SIAM J. APPLIED DYNAMICAL SYSTEMS, Vol. 20, No. 2, pp. 1135–1157, **Society for Industrial and Applied Mathematics**, 2021
- [50] Chongli Jiang *Mathematical Mechanism of Quarantine Measures for SARS Epidemic, The first International Conference on Algebraic Biology* Japan (2005)
- [51] Timothy C. Germann and al., Mitigation strategies for pandemic influenza in the United States **PNAS** (2006) Medical Sciences series, 103; 5935-5940