MATH 4010/6010: Mathematical Biology

Instructor: Remus Oșan, Georgia State University

Lecture 1 – May 19, 2014

Introduction and course overview

A first example
Introduction

- Remus Oșan: rosan@bu.edu, http://www2.gsu.edu/~rosan/math_bio_romania_2014.html
- Assistant Professor, Dept. Mathematics and Statistics, Neuroscience Institute, Georgia State University
- Romanian organizer: Assist.Prof.Eng. Ioan Muntean
- Computer Science, U. Tehnica Cluj
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Introduction

- Remus Oşan:
  - **Research**: Development of analysis methods for neural data
  - Data-driven computational modelling for sensory and memory systems in the brain, neural development and regeneration
Introduction

- Course Hours:
  - 10 – 12, 2-3 pm Mon/Wed
  - 10 – 12, 2-4 pm Tue/Th

- Location
  - Baritiu 26-28, sala S4.1 (corp cladire Somes, etaj 4)
Textbook

- Edelstein-Keshet, Mathematical Models in Biology.
- Plan to Cover chapters 1 – 8
Evaluation of course performance

- Final grade will be assigned base on
- Homework: 4 hws, lowest one dropped (~ 2 per week)
- Each one counts as 15 percent of the grade (40 overall)

- Final: last week (June 4, tentatively): 35 percent
- Class project: June 4 project presentation: 20 percent
  implement and investigate a mathematical model OR read and critically evaluate a set of papers

Math Bio Cluj 2014 – Lect 1, May 19
Course material

• 1 Discrete processes
• Chapter 1: Linear difference equations
• Nth order difference equations, systems of difference equations, real and complex eigenvalues and their qualitative meaning.
• Applications: Fibonacci numbers and patterns in nature, segmental growth, carbon dioxide and breathing.
Finite difference equations

- Chapters 2,3: Introduction to nonlinear difference equations
- Steady states, stability, bifurcation values
- Behavior of the logistic equation, chaotic solutions
- Stability calculations for second order equations
- Scaling and parameter reduction
- Applications: spread of disease, host-parasite systems, populations genetics
II Continuous processes and ordinary differential equations (ODEs)

- Chapter 4: Introduction to continuous models
- Review of linear ODEs, comparison to difference equations, stability
- Dimensional analysis
- Applications: behavior of chemostat, drugs given by continuous infusion, glucose-insulin kinetics, compartmental analysis.
II Continuous processes and ordinary differential equations (ODEs)

• Chapter 5: Phase-plane methods and qualitative solutions
• Vector fields, nullclines, heteroclinic and homoclinic orbits, constructing global
• Phase planes. Is a whole small course!
• Applications: chemostat, more on control of breathing.
II Continuous processes and ordinary differential equations (ODEs)

• Chapter 6: Applications to population dynamics
• Predator-prey systems
• Populations in competition
• Population biology of infectious diseases
## II Continuous processes and ordinary differential equations (ODEs)

- Chapter 7: Models of molecular events
- Michaelis-Menton kinetics
- Singular perturbation ideas and quasi-steady-state analysis.
- Cooperative reactions
- Morphogenesis and a molecular switch
- Activator-inhibitor and positive feedback systems
II Continuous processes and ordinary differential equations (ODEs)

- Chapter 8: Limit cycles, oscillation and excitable systems
- Hodgkin-Huxley nerve conduction equations (derivation and some analysis)
- FitzHugh Nagumo simplification
- Hopf bifurcations
- Oscillations in chemical systems
Additional Textbooks

- A Course in Mathematical Biology: Quantitative Modeling with Mathematical and Computational (Monographs on Mathematical Modeling and Computation) (Paperback)
- Gerda de Vries, Thomas Hillen, Mark Lewis, Johannes Muller, Birgitt Schonfisch
Additional Textbooks

- An Introduction to Mathematical Biology, by Linda Allen
Additional Textbooks

- Mathematical Foundations of Neuroscience (Interdisciplinary Applied Mathematics)
  - G. Bard Ermentrout,
  - David H. Terman
Additional Textbooks

• Mathematical Biology: I. An Introduction (Interdisciplinary Applied Mathematics) (Pt. 1)
  by James D. Murray
Course software

- Matlab ([www.mathworks.com](http://www.mathworks.com))
- Mathematica ([www.wolfram.com](http://www.wolfram.com))
- Not a requirement for the course evaluations
- Hw solutions make use of these packages

- dfield and pplane (phase field visualization) ([http://math.rice.edu/~dfield/dfpp.html](http://math.rice.edu/~dfield/dfpp.html))
Aims of course

• Learn to formulate mathematical descriptions for biological systems

• Learn techniques for analyzing such descriptions

• Develop ability to be thoughtful about where the mathematics can be helpful: what does a model tell us about the system that we didn’t know before.
Short overview

• Success stories in mathematical biology
• Still very much an evolving field

• Mathematical methods used in the life science models
• Keep it relatively simple
Short overview

- One fundamental property of the biological systems is their high level of complexity, with interactions spanning different spatial and temporal timescales.

- In order to conduct meaningful modeling, the system almost always need to be simplified, otherwise the mathematics become too complex.
Short overview

• Renewed interest in mathematical models in life sciences
• More experimental data: genomics, neural recordings, large-scale medical/social studies

• Limitations of things one can do in an experimental setting: mathematical models (more powerful computational technologies)
Short overview

• Techniques used in this class
  – linear difference equations,
  – non-linear difference equations,
  – single and systems of ordinary differential equations
  – phase plane analysis

• Capture the qualitative behavior exhibited by the biological systems
Short overview

• The modeling process
  – Posing a question
  – Determine the important components that affect the behavior of a system.

• A model is then constructed

• Interactions between all model components
Short overview

• Why bother doing mathematical modeling?

• Framework for understanding the data

• Account for missing data

• Confirm/reject hypothesis

• Make prediction for untested conditions and different parameters

• Formulate new hypotheses
Short overview

• Models can be simple in nature

• Ignore small details, focus on the large picture

• One cannot have a perfect model (think that it results from fitting data)

• Models can be made increasingly complex at the expense of large-scale simulations
Some simple examples

- Simplest equation
- $x_{n+1} = x_n + 1$ – reduces to counting

- Earning a salary
- $x_{n+1} = x_n + 10k$ – more elaborate counting

- Investment banking:
- $x_{n+1} = x_n + 0.05 \times x_n$
Some simple examples

- $X_{n+1} = x_0 \times 1.05^{n+1}$
- Applies to banking, Ponzi schemes, vampires (see Transylvania) and zombies
- Assumes unlimited growth (right)

- $X_{n+1} = x_0 \times 2^{n+1}$ – the chess legend
Success stories in math bio

- Population ecology
- Cycles in the predator-prey populations

- Write a simple model for each population
Predator-prey systems

• Rabbits multiply (depends the overall population)
• Rabbits die
• Rabbits are hunted by lynxes

• Lynxes multiply (depend on the population size and the available food – rabbits)
• Lynxes die too
Neural dynamics

• Hodgkin and Huxley (1950)
• First model that captured the dynamics of cell membrane action potentials
• Nobel prize, created a new field of mathematics
Development of neural maps

• Sur Lab (MIT) – 2000
• Rewiring Cortex: Functional Plasticity of the Auditory Cortex

• Experiment
• Model
Reaction-diffusion patterns

- Tiger, Leopard, Giraffe, Zebra
- Spatially distributed models that reproduce the patterns seen in nature (Alan Turing, 1952, morphogenesis)

- Is this the real mechanism?
- Useful to have models that can be tuned to obtain all the observed patterns.
Epidemiology models

- The SIR model,
- S (for susceptible),
- I (for infectious)
- R (for recovered)
Introduction

• Let us introduce some simple example as well

• Start at the basics and aim to cover the more complicated examples...

• 1.1 BIOLOGICAL MODELS USING DIFFERENCE EQUATIONS - *Cell Division*
1.1 Biological models using difference equations

- *Cell Division* – for example bacteria

- Do all cells divide at the same time?
- Probably not

- To keep things simple we will assume that all cells divide synchronously producing daughter cells
1.1 Difference equations: cell division

• **Questions**: how many cells exist at a certain moment in time?

• **Answer**: Observational study, just do the experiment

• **Q**: What if the experiment is expensive?
• **A**: Building a model for guidance is advised.
1.1 Difference equations: cell division

• **Some definitions:**
  
  • Define the number of cells in each generation with a subscript
  
  • $M_0$ initial population
  
  • $M_1, M_2, \ldots, M_n$ are respectively the number of cells in the first, second, \ldots, $n^{th}$ generations

• How fast is the population increasing?
1.1 Difference equations: cell division

• Mathematical model:
  \[ M_{n+1} = a \, M_n \]

• **Q:** Why do we choose this model?

• **A:** Simple
  
  • **A:** Agrees with our understanding of the data
1.1 Difference equations: cell division

- Mathematical model: $M_{n+1} = a M_n$
- $Q$: What are the implication of the model?
- $A$: The number of cells in the new generations is completely determined. We can find out the general formula by looking at the equation in more detail.
- $M_1 = a M_0$ (we know $M_0$, so now we know $M_1$)
1.1 Difference equations: cell division

- $M_1 = a \ M_0$;  \[ M_2 = a \ M_1 = a \ (a \ M_0) = a^2 \ M_0 \]

- By now the procedure is clear
- $M_3 = a \ M_2 = a \ (a^2 \ M_0) = a^3 \ M_0$

- In general: $M_n = a^n \ M_0$

- Proof by induction
1.1 Difference equations: cell division

- Initial population size: $M_0$
- Parameter of the models:
  - $a$ – number of daughters per cell
- We can compute $M_n$:
  - the number of cells at generation $n$
- Much faster than doing the experiment
1.1 Difference equations: cell division

- Example: $M_0 = 100, a = 2$

- $M_{10} = a^{10} \cdot 100 = 1024 \cdot 100 = 102,400$

- What are the long-term prospects for this population?
  - Decline
  - Explode
  - Stay the same
1.1 Difference equations: cell division

- $|a| > 1$ – Explodes (we ignored limiting factors)
- $M_n$ increases over successive generations

- $|a| < 1$ (Extinct: $a_n \to 0$ as $n \to \infty$)
- $M_n$ decreases over successive generations

- $a = 1$ ($a_n = 1$, equilibrium, in balance)
- $M_n$ is constant.
1.1 Difference equations: Rabbits!!

- Nothing reproduces faster than rabbits (this is an exaggeration)

- Assume one wants to determine the total number of unchecked rabbits
1.1 Difference equations: Rabbits!!!

- The reproduction of rabbits captured the Fibonacci’s imagination in the year 1202
- Presumably he could not investigate the natural system in detail
- He created a set of rules describing the ideal conditions for rabbits breeding
- Then Fibonacci determined the expected number of rabbits as a function of time
1.1 Difference equations: Rabbits!!!

• How many pairs of rabbits can be produced from one pair in a year if it is supposed that every month each pair begets a new pair which from the second month on becomes productive?

• Rabbits do not start producing until they are 2 months old, and then keep on producing forever (or at least beyond the year.)
1.1 Difference equations: Rabbits!!!

- 1. You begin with one male rabbit and one female rabbit. These rabbits have just been born.
- 2. A rabbit will reach sexual maturity after one month.
- 3. The gestation period of a rabbit is one month.
- 4. Once it has reached sexual maturity, a female rabbit will give birth every month.
- 5. A female rabbit will always give birth to one male rabbit and one female rabbit.
- 6. Rabbits never die.
1.1 Difference equations: Rabbits!!!

- Counting the rabbits

You start with one pair of rabbits (Original Pair)
Each white pair is a new pair, and can't yet breed
Each brown pair is a mature pair, and can breed
Each column represents one month
The pairs going straight across are the same pair each month
As you can see, the rabbits multiply to the Fibonacci Sequence

• 1 1 2 3 5 8
1.1 Difference equations: Rabbits!!!

- Define $R_n^0$ as # of newborn pairs in month $n$.
- $R_n^1 =$ # 1-month old in month $n$ etc.
- Superscript = age of the rabbits in months
- Subscript = month in question.

- Note that $R_n^1 = R_{n-1}^0$.
- number of rabbit pairs of age 1 month at some time is the number just born the month before.
1.1 Difference equations: Rabbits!!!

- Similarly $R_n^2 = R_{n-2}^0$

- the number of rabbit pairs of age 2 month at some time is the number just born two months before.

- Assumption: $R_n^0 = R_n^2 + R_n^3 + R_n^4 + \ldots$ until the numbers on the RHS are zero.
1.1 Difference equations: Rabbits!!!

- \( R_n^0 = R_n^2 + R_n^3 + R_n^4 + \ldots \)
- We seek something that looks like Fibonacci series (since he got famous with this equation in the meantime)

- \( R_n^0 = R_{n-1}^0 + R_{n-2}^0 \)
- The first equation is very different from the second!
- Where does the Fibonacci equation come from?
1.1 Difference equations: Rabbits!!!

- Try rewriting the equation above just with changes indices, using the fact that the above is correct for any \( n \):

\[
\begin{align*}
R_n^0 &= R_n^2 + R_n^3 + R_n^4 + \ldots \\
R_{n-1}^0 &= R_{n-1}^2 + R_{n-1}^3 + R_{n-1}^4 + \ldots = R_n^3 + R_n^4 + R_n^5 + \ldots \\
\text{Subtract the two equations: } R_n^0 - R_{n-1}^0 &= R_n^2
\end{align*}
\]
1.1 Difference equations: Rabbits!!!

- We obtained: $R_n^0 - R_{n-1}^0 = R_n^2$

- Now use the fact that $R_n^2 = R_{n-1}^1 = R_{n-2}^0$

- Voila: $R_n^0 = R_{n-1}^0 + R_{n-2}^0$

- The Fibonacci series
1.1 Difference equations: Rabbits!!!

- This problem has an alternative formulation: Problem 14 from pages 32-33

- Rabbits reproduce only twice
- At ages 1 mo and 2 months
- Produce only one pair of rabbits.
- None of them die.
- In generation 1, there is one pair.
1.1 Difference equations: Rabbits!!!

- At first glance there are fewer rabbits
- Since the rabbits do not reproduce forever
- However these rabbits have a head start
- They start reproducing at an earlier age, namely at month 1

- Who has the ‘advantage’?
1.1 Difference equations: Rabbits!!

- Use the same definitions

- Define $R_n^0$ as # of newborn pairs in month $n$.  
  - $R_n^1 = \#$ 1-month old in month $n$ etc.

- Superscript stands for the age of the rabbits in months
- Subscript for the month in question.
1.1 Difference equations: Rabbits!!!

- It is easier to write the solution for this problem.
- The number of newborn pairs equals the number of 1-month old and 2 month olds.
- \( R_n^0 = R_n^1 + R_n^2 = R_{n-1}^0 + R_{n-2}^0 \).
- One adds up the previous numbers of newborns from the past 2 months to get the number of newborns for the current month.
- Done. Fibonacci series.
1.1 Difference equations: Rabbits!!

- We can still count them in a formal way:
- Month 1: Starting with one pair of rabbits
- \( R_0^0 = 1 \).

- Month 2: The rabbits have mated, but there are no newborns yet:
- \( R_1^1 = 1, \ R_1^0 = 0 \)
1.1 Difference equations: Rabbits!!!

- Month 3: A new pair of rabbits is born; the old pair is 2 months old:
  - $R_2^2 = 1,$
  - $R_2^1 = 0,$
  - $R_2^0 = 1$
1.1 Difference equations: Rabbits!!!

- Month 4: A new pair of rabbits is born; the oldest pair is 3 months old, second generation is mating:
- $R_3^3 = 1, R_3^2 = 0, R_3^1 = 1, R_3^0 = 1$
1.1 Difference equations: Rabbits!!

- Month 5: Two new pairs of rabbits are born
  - $R_4^4 = 1$,
  - $R_4^3 = 0$,
  - $R_4^2 = 1$,
  - $R_4^1 = 1$,
  - $R_4^0 = 2$
1.1 Difference equations: Rabbits!!!

- Month 3: A new pair of rabbits is born; the old pair is 2 months old:
  \[ R_2^2 = 1, \ R_2^1 = 0, \ R_2^0 = 1 \]

- Month 4: A new pair of rabbits is born; the oldest pair is 3 months old, second generation is mating:
  \[ R_3^3 = 1, \ R_3^2 = 0, \ R_3^1 = 1, \ R_3^0 = 1 \]

- Month 5: Two new pairs of rabbits are born
  \[ R_4^4 = 1, \ R_4^3 = 0, \ R_4^2 = 1, \ R_4^1 = 1, \ R_4^0 = 2 \]
1.1 Difference equations: Rabbits!!!

• Summing up the total number of rabbits gives us the Fibonacci sequence: 1, 1, 2, 3, 5, 8, 13, ...

• Can we solve and obtain an analytical formula for this series?

• Formally we have this equation: $x_{n+2} = x_{n+1} + x_n$
  • Where $x_n = R_n^0$
1.1 Linear difference equations

- Actually let’s take this one step further and consider the more general equation:
  \[ x_{n+2} + a x_{n+1} + b x_n = 0 \]

- Solution for this equation depends on the eigenvalues, which are the roots of the characteristic equation:
  \[ x^2 + a x + b = 0 \]
1.1 Linear difference equations

• Compute the roots of the characteristic equation \( x^2 + a \cdot x + b = 0 \)

\[
\phi = \left( -a - \sqrt{a^2 - 4b} \right) / 2
\]

\[
\mu = \left( -a + \sqrt{a^2 - 4b} \right) / 2
\]

• Turns out that the complete solution is:

• \( x_n = c_1 \phi^n + c_2 \mu^n \)
1.1 Linear difference equations

- For the rabbit problem $a = 1$ and $b = -1$, therefore

\[ \phi = \left(1 + \sqrt{5}\right)/2 \approx 1.6180 \]
\[ \mu = \left(1 - \sqrt{5}\right)/2 \approx -0.6180 \]

- Hence the number of rabbits in month $n$ is:
  - $x_n = c_1 \phi^n + c_2 \mu^n = c_1 1.618^n + c_2 (-0.618)^n$
1.1 Linear difference equations

• The number of rabbits in month $n$ is:

$$x_n = c_1 \phi^n + c_2 \mu^n = c_1 \ 1.618^n + c_2 \ (-0.618)^n$$

• Are we done here?

• No, we still need to determine the coefficients $c_1$ and $c_2$

• Need to use what we know about the initial conditions: $x_0 = 1$, $x_1 = 1$, $x_2 = 2$
1.1 Linear difference equations

• How to find specific solutions, given initial conditions.

• Get two equations for unknowns $c_1$ and $c_2$ by plugging in for $x_0$ with $n = 0$ and $x_1$ for $n = 1$.

• Note that need exactly two terms in the series to get all the terms after it.
1.1 Linear difference equations

- Write down the system of equations and solve it.

\[
\begin{cases}
  x_0 = c_1 \mu^0 + c_2 \phi^0 \\
  x_1 = c_1 \mu^1 + c_2 \phi^1
\end{cases}
\]

- We obtain:

\[
\begin{cases}
  c_1 = (\phi - 1)/(\phi - \mu) \approx 0.2764 \\
  c_2 = (1 - \mu)/(\phi - \mu) \approx 0.7236
\end{cases}
\]
1.1 Linear difference equations

• We finally obtain the following formula:

\[ x_n = 0.7236 \cdot 1.618^n + 0.2736 \cdot (-0.618)^n \]

\[ x_n = \frac{1 - \mu}{\phi - \mu} \cdot \phi^n + \frac{\phi - 1}{\phi - \mu} \mu^n \]
1.1 Linear difference equations

- Can we make additional use of this formula?

\[ x_n = 0.7236 \cdot 1.618^n + 0.2736 \cdot (-0.618)^n \]

\[ x_n = \frac{1 - \mu}{\phi - \mu} \cdot \phi^n + \frac{\phi - 1}{\phi - \mu} \mu^n \]

- Yes, we can use it for a quick estimate for the TOTAL NUMBER of rabbits when \( n \) (the number of months) is large
1.1 Linear difference equations

- Quick estimate at large numbers
  \[ x_n = 0.7236 \cdot 1.618^n + 0.2736 \cdot (-0.618)^n \]

- Idea: solution is \( c_1 \varphi^n + c_2 \mu^n \), where \( \mu \) is negative and \( < 1 \) in absolute value.

- Hence, for \( n \) large, the second term hardly matters.
1.1 Linear difference equations

• So we have to add up the number of newborns from month 0 thru month N

• Approximately $c_1(1 + \varphi + \varphi^2 + \ldots + \varphi^n) = c_1 S$.

• Geometrical series $= (\varphi^n - 1)/(\varphi - 1)$

• Total number of rabbits $= c_1(\varphi^n - 1)/(\varphi - 1)$
1.1 Linear difference equations

• Also, the exact formula is the sum of two geometrical series.

• The problem is that the second term oscillates between positive and negative values, but decays to zero.

• Hence is dominated by the first term which grows exponentially.
1.1 Linear difference equations

- **Other problems** with the formulations (e.g. future directions)

- Where does the first pair come? Wrong question for this class, we just assume it.

- There are genetics concerns if we start with one pair for breeding. Let’s assume a larger initial population, and not immediate family breeding and this can be addressed.
1.1 Linear difference equations

• **Other problems** with the formulations (e.g. future directions)

• How about the ratio of male/females in each generation being equal to 1?
• This is probably not right, and also the number of offsprings is generally greater than two and varies.
• Putting randomness in the formulas is a big problem for obtaining analytical results.
1.1 Linear difference equations

- According to wiki,
- Humans have a Fisherian sex ratio.
- In humans the secondary sex ratio is commonly assumed to be 105 boys to 100 girls
1.1 Linear difference equations

- Traditionally, farmers have discovered that the most economically efficient community of animals will have a large number of females and a very small number of males.
- A herd of cows and a few prize bulls or a flock of chickens and one rooster are the most economical sex ratios for domesticated livestock.
- [http://en.allexperts.com/e/s/se/sex_ratio.htm](http://en.allexperts.com/e/s/se/sex_ratio.htm)
1.1 Linear difference equations

- Elephants reproduce well and in approximately even numbers in the wild
- Skewed birth sex ratio in captivity (0.71)
1.1 Linear difference equations

- The Fibonacci Spiral is a geometric spiral whose growth is regulated by the Fibonacci Series.

- Its sudden, almost exponential growth parallels the rapid growth of the series itself.

- The spiral itself is a series of connected quarter-circles drawn inside an array of squares with Fibonacci numbers for dimensions.
1.1 Linear difference equations

- The Fibonacci Spiral
1.1 Linear difference equations

- The Fibonacci number: golden ratio
1.1 Linear difference equations

- Another notable example is human body.
- In human body, the ratio of the length of forearm to the length of the hand is equal to 1.618, that is, Golden Ratio.
1.1 Linear difference equations

• Another well-known examples on human body are:
  – The ratio between the length and width of face
  – Ratio of the distance between the lips and where the eyebrows meet to the length of nose
  – Ratio of the length of mouth to the width of nose
1.1 Linear difference equations

• Another well-known examples on human body are:
  – Ratio of the distance between the shoulder line and the top of the head to the head length
  – Ratio of the distance between the navel and knee to the distance between the knee and the end of the foot
  – Ratio of the distance between the finger tip and the elbow to the distance between the wrist and the elbow
1.1 Linear difference equations

- Fibonacci numbers or patterns are found in:
  - Sea Shells
  - Petals on Flowers
  - Sunflower seed Heads
  - Pine Cones, Palms
  - Pineapple and other Bromeliads
  - Plant Growth or leaf/petal arrangements in 90% of plants.
1.1 Linear difference equations

- The same happens in many seed and flower heads in nature.
- The reason seems to be that this arrangement forms an optimal packing of the seeds so that, no matter how large the seed head, they are uniformly packed at any stage, all the seeds being the same size, no crowding in the centre and not too sparse at the edges.
1.1 Linear difference equations

- [http://britton.disted.camosun.bc.ca/fibslide/jbfibslide.htm](http://britton.disted.camosun.bc.ca/fibslide/jbfibslide.htm)
1.6 QUALITATIVE BEHAVIOR OF SOLUTIONS TO LINEAR DIFFERENCE EQUATIONS

- Linear difference equations are characterized by the following properties
- 1. An $m^{th}$-order equation:
  $$a_0 x_n + a_1 x_{n-1} + \ldots + a_m x_{n-m} = b_m$$
- 2. The *order* $m$ of the equation is the number of previous generations that directly influence the value of $x$ in a given generation.
1.6 QUALITATIVE BEHAVIOR OF SOLUTIONS TO LINEAR DIFFERENCE EQUATIONS

• 3. When

\[ a_0, a_1, \ldots, a_m = \text{constant}, \ b_m = 0 \]

• constant-coefficient homogeneous linear difference equation
• Solutions are of linear combinations of:
• \[ x_n = C \lambda^n \]
1.6 QUALITATIVE BEHAVIOR OF SOLUTIONS TO LINEAR DIFFERENCE EQUATIONS

4. We can solve for \( \lambda \) using the following equation:

\[
a_0 \lambda^m + a_1 \lambda^{m-1} + \ldots + a_m = 0
\]

5. First-order equation has one solution

Second-order equation has two solutions.

In general, an \( m^{\text{th}} \)-order equation has \( m \) basic solutions.
1.6 QUALITATIVE BEHAVIOR OF SOLUTIONS TO LINEAR DIFFERENCE EQUATIONS

• 6. The general solution is a linear superposition of the \( m \) basic solutions of the equation

• 7. For real values of \( \lambda \) the qualitative behavior of a basic solution depends on whether \( \lambda \) falls into one of four possible ranges: (provided all values of \( \lambda \) are distinct).

• \( \lambda \geq 1, \lambda \leq -1, 0 < \lambda < 1, -1 < \lambda < 0. \)
1.6 QUALITATIVE BEHAVIOR OF SOLUTIONS TO LINEAR DIFFERENCE EQUATIONS

- (a) For $\lambda > 1$, $\lambda^n$ grows as $n$ increases;
- thus $x_n = C \lambda^n$ grows without bound.
1.6 QUALITATIVE BEHAVIOR OF SOLUTIONS TO LINEAR DIFFERENCE EQUATIONS

• (b) For $0 < \lambda < 1$, $\lambda^n$ decreases to zero with increasing $n$; thus $x_n$ decreases to zero.
1.6 QUALITATIVE BEHAVIOR OF SOLUTIONS TO LINEAR DIFFERENCE EQUATIONS

- (c) For $-1 < \lambda < 0$, $\lambda^n$ oscillates between positive and negative values while declining in magnitude to zero.
1.6 QUALITATIVE BEHAVIOR OF SOLUTIONS TO LINEAR DIFFERENCE EQUATIONS

- (d) For $\lambda < -1$, $\lambda^n$ oscillates as in (c) but with increasing magnitude.
1.1 Linear difference – segmental growth

- **Problem 1: Growth of Segmental Organisms**
- **Page 26 from** Edelstein-Keshet book (also Problem 15/page 33)
- Hypothetical situation arises in organisms such as certain filamentous algae and fungi that propagate by addition of segments.
- The rates of growth and branching may be complicated functions of densities, nutrient availability, and internal reserves.
1.1 Linear difference – segmental growth

- Simplified version of this phenomenon for illustration purposes
- Prove versatility of difference equation models.
- A segmental organism grows by adding new segments at intervals of 24 hours in several possible ways
1.1 Linear difference – segmental growth

- 1. A terminal segment can produce a single daughter with frequency $p$, thereby elongating its branch.
- 2. A terminal segment can produce a pair of daughters (dichotomous branching) with frequency $q$.
- 3. A next-to-terminal segment can produce a single daughter (lateral branching with frequency $r$.)
1.1 Linear difference – segmental growth

The question to be addressed is how the numbers of segments change as this organism grows.

In approaching the problem, it is best to define the variables depicting the number of segments of each type (terminal and next-to-terminal), to make several assumptions and to account for each variable in a separate equation.
1.1 Linear difference – segmental growth

• Let us use the following notations

• $a_n = \text{number of terminal segments}$,
• $b_n = \text{number of next-to-terminal segments}$,
• $S_n = \text{total number of segments}$. 
1.1 Linear difference – segmental growth

- **Assumptions:**
  - All daughters are terminal segments;
  - All terminal segments participate in growth ($p + q = 1$) and thereby become next-to-terminal segments in a single generation;
  - All next-to-terminal segments are thereby displaced and can no longer branch after each generation.
1.1 Linear difference – segmental growth

• Show that equations for $a_n$ and $b_n$ can be combined to give:
  $$a_{n+1} - (1 + q)a_n - r a_{n-1} = 0,$$
• Explain the equation.

• $p$ = fraction of end segments that have one bud next generation;
• $q$ = fraction with 2 buds on end segments; $p+q = 1$.
• $r$ = fraction of next to end segments that bud
1.1 Linear difference – segmental growth

• The growth equations then becomes:

\[ a_{n+1} = a_n p + 2 a_n q + b_n r \]
\[ b_{n+1} = a_n \]
\[ s_{n+1} = s_n + a_n p + 2 a_n q + b_n r \]
1.1 Linear difference – segmental growth

• Solving for $a_n$ yields: $a_{n+1} = (p + 2q) a_n + r a_{n-1}$

• Using $p + q = 1$, it follows that the equations for $a_n$ and $b_n$ can be combined to give:

• $a_{n+1} - (1 + q) a_n - r a_{n-1} = 0$

• Use initial conditions: $a_1 = 1, b_1 = 0$, so $a_0 = 0$. 
1.1 Linear difference – segmental growth

- A numerical example for p = ½, q = ½ and r = ½.

<table>
<thead>
<tr>
<th>(a_n)</th>
<th>(b_n)</th>
<th>(S_n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0000</td>
<td>0</td>
<td>1.0000</td>
</tr>
<tr>
<td>1.5000</td>
<td>1.0000</td>
<td>2.5000</td>
</tr>
<tr>
<td>2.8000</td>
<td>1.5000</td>
<td>5.3000</td>
</tr>
<tr>
<td>4.9000</td>
<td>2.8000</td>
<td>10.1000</td>
</tr>
<tr>
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<tr>
<td>27.5000</td>
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</tr>
<tr>
<td>49.1000</td>
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<tr>
<td>87.4000</td>
<td>49.1000</td>
<td>198.2000</td>
</tr>
<tr>
<td>155.6000</td>
<td>87.4000</td>
<td>353.8000</td>
</tr>
</tbody>
</table>
1.1 Linear difference – segmental growth

- A numerical example for \( p = \frac{1}{2}, q = \frac{1}{2} \) and \( r = \frac{1}{2} \).
1.1 Linear difference – segmental growth

- Example: Simulating colonial growth of fungi with the Neighbour-Sensing model of hyphal growth, Audrius Meškauskas1, Mark D. Fricker2 and David Moore1, Mycological Research, Volume 108, Issue 11, November 2004, Pages 1241-1256
Topics covered so far

• Introduction in mathematical models in life sciences
• Linear difference equation
  – Cell division
  – Rabbits problem (Fibonacci numbers)
  – Segmental growth model
• Matlab overview
  – Obtaining and plotting solutions with Matlab
1.1 Linear difference – Red blood cells

- A Schematic Model of Red Blood Cell Production

- Number of red blood cells (RBCs) circulating in the blood – approx $2–3 \times 10^{13}$ according to wiki
- 25% of the total human body cell number
- Each circulation takes about 20 seconds
- Each cell lives approx 100–120 days in the body
1.1 Linear difference – Red blood cells

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1.1 Linear difference – Red blood cells

- Reticuloendothelial system (spleen, liver and bone marrow)
- Removes old or defective cells, continually replenishing the cell count
- Normally occurs at the same rate of production, balancing the total numbers.

http://www.nature.com/nature/journal/v420/n6917/fig_tab/nature01321_F1.html
1.1 Linear difference – Red blood cells

• Blood doping – collect blood cells, freeze and reintroduce them into the system, difficult to detect

• Risk of infections, increase viscosity of blood (may lead to heart failure)

• Replaced by genetic engineering: Athletes may simply inject erythropoetin (EPO), which causes the body to make the cells

• Identical to natural chemicals made by the body - making sure detection difficult or impossible

• [http://whyfiles.org/090doping_sport/3.html](http://whyfiles.org/090doping_sport/3.html)
1.1 Linear difference – Red blood cells

- In the circulatory system, the red blood cells (RBCs) are constantly being destroyed and replaced.
- Since these cells carry oxygen throughout the body, their number must be maintained at some fixed level.
- Assume that the spleen filters out and destroys a certain fraction of the cells daily and that the bone marrow produces a number proportional to the number lost on the previous day.
1.1 Linear difference – Red blood cells

• **Questions:** What is the number of red cells at a certain moment in time?

• **Answer:** Build a mathematical model

• 1) Assume discrete time
• 1 basic unit of time = 1 day

• Define variables
1.1 Linear difference – Red blood cells

2) Variables:
- \( R_n \) = # of RBCs in circulation on day n,
- \( M_n \) = # of RBCs produced by marrow on day n

3) Parameters
- \( f \) = fraction RBCs removed by spleen,
- \( \gamma \) = production constant (# produced per # lost).
1.1 Linear difference – Red blood cells

- 4) variables and parameters → equations
  - \( R_{n+1} = R_n - f R_n + M_n \)

- RBC in day \( n + 1 \) = RBC in day \( n \) – RBC removed by spleen in day \( n \) + RBC produced by marrow in day \( n \)

- \( M_{n+1} = \gamma f R_n \)
- RBC produced by marrow in day \( n + 1 \) = fraction RBCs removed by spleen x marrow RBC in day \( n \)
1.1 Linear difference – Red blood cells

- After simplifications, we obtain the following system of equations:

- \( R_{n+1} = (1 - f) R_n + M_n \)
- \( M_{n+1} = \gamma f R_n \)

- A coupled \( (R_{n+1} \text{ depends on } M_n) \) system of two linear 1st order difference equations
1.1 Linear difference – Red blood cells

• **Q:** How do we solve this system of eqs?
• **A:** One option is to use substitution.

• \( R_{n+1} = (1 - f) R_n + M_n \)
• \( M_{n+1} = \gamma f R_n \)

• \( R_{n+2} = (1 - f) R_{n+1} + M_{n+1} = (1 - f) R_{n+1} + \gamma f R_n \)
• Second order linear difference equation
1.1 Linear difference – Red blood cells

• We had a similar example for the segmental growth problem \((a_{n+1} - (1 + q) a_n - r a_{n-1} = 0)\)

• How do we solve this type of equation:
  • \(x_{n+1} + a x_n + b x_{n-1} = 0\)

• Guess a solution: \(x^n = c \lambda^n\)
1.1 Linear difference – Red blood cells

- $x_{n+1} + a x_n + b x_{n-1} = 0$
- Guess a solution: $x^n = c \lambda^n$
- Substitute in: $c \lambda^{n+1} + a c \lambda^n + b c \lambda^{n-1} = 0$
- The parameter $c$ cancels out
- $\lambda^{n+1} + a c \lambda^n + b c \lambda^{n-1} = 0$
- $\lambda^{n-1} (\lambda^2 + a \lambda + b) = 0$
- The characteristic equation corresponding to the general equation is: $\lambda^2 + a \lambda + b = 0$
1.1 Linear difference – Red blood cells

• For our problem:

\[ R_{n+2} = (1 - f) R_{n+1} + M_{n+1} = (1 - f) R_{n+1} + \gamma f R_n \]

• \( a = -(1 - f), \ b = -\gamma f \)

• We then obtain

\[ \lambda_{1,2} = \frac{(1 - f) \pm \sqrt{(1 - f)^2 + 4\gamma f}}{2} \]

• The general solution is then:

\[ R_n = C_1 \lambda_1^n + C_2 \lambda_2^n \]
1.1 Linear difference – Red blood cells

- An analytical solution!

\[ R^n = C_1 \left( \frac{(1 - f) + \sqrt{(1 - f)^2 + 4\gamma f}}{2} \right)^n + C_2 \left( \frac{(1 - f) - \sqrt{(1 - f)^2 + 4\gamma f}}{2} \right)^n \]

- Difference equation is linear
- \( C_1 \lambda_1^n \) and \( C_2 \lambda_2^n \) are solutions
- Their sum is also a solution
- We can determine \( C_1 \) and \( C_2 \) from \( R_0 \) and \( R_1 \)
1.1 Linear difference – Red blood cells

- Let’s determine $C_1$ and $C_2$ from $R_0$ and $R_1$

\[
\begin{align*}
R_0 &= c_1 \lambda_1^0 + c_2 \lambda_2^0 \\
R_1 &= c_1 \lambda_1^1 + c_2 \lambda_2^1
\end{align*}
\]

\[
\begin{align*}
R_0 &= c_1 + c_2 \\
R_1 &= c_1 \lambda_1 + c_2 \lambda_2
\end{align*}
\]

\[
\begin{align*}
c_2 &= R_0 - c_1 \\
R_1 &= c_1 \lambda_1 + (R_0 - c_1) \lambda_2
\end{align*}
\]

\[
\begin{align*}
c_2 &= c_1 - R_0 \\
R_1 &= c_1 (\lambda_1 - \lambda_2) + R_0 \lambda_2
\end{align*}
\]

\[
\begin{align*}
c_2 &= c_1 - R_0 \\
c_1 &= \frac{R_1 - R_0 \lambda_2}{\lambda_1 - \lambda_2}
\end{align*}
\]

\[
\begin{align*}
c_2 &= R_0 - \frac{R_1 - R_0 \lambda_2}{\lambda_1 - \lambda_2} \\
c_1 &= \frac{R_1 - R_0 \lambda_2}{\lambda_1 - \lambda_2}
\end{align*}
\]
1.1 Linear difference – Red blood cells

- Finally the solution for $C_1$ and $C_2$

$$
\begin{align*}
    c_2 &= \frac{-R_1 + R_0 \lambda_1}{\lambda_1 - \lambda_2} \\
    c_1 &= \frac{R_1 - R_0 \lambda_2}{\lambda_1 - \lambda_2}
\end{align*}
$$

- Use numerical example with $f = 0.01$, $\gamma = 1$, $R_0 = 1000$, $M_0 = 10$
1.1 Linear difference – Red blood cells

- Numerical example
- \( f = 0.1, \gamma = 1, R_0 = 1000, M_0 = 10 \)

- Run matlab script rbc.m
1.1 Linear difference – Red blood cells

• Let’s look at another way to solve this equation
• The new approach is more general and will work for more complicated cases
• We’ll think about the system as two 1st order equations (We don’t combine)

• We’ll use concepts from linear algebra
• Linear algebra review
1. 4 Linear algebra review

• Consider the following system of linear algebraic equation

\[
\begin{align*}
  a_{11}x + a_{12}y &= 0 \\
  a_{21}x + a_{22}y &= 0
\end{align*}
\] (1)

• Note we don’t have difference equations here (that is no n, n+1 indices, etc)

• Rewrite in vector notations
1. 4 Linear algebra review

• Two by two matrix multiplied by 2x1 vector = 2x1 vector

\[
\begin{pmatrix}
a_{11} & a_{12} \\
a_{21} & a_{22}
\end{pmatrix}
\begin{pmatrix}
x \\
y
\end{pmatrix} =
\begin{pmatrix}
0 \\
0
\end{pmatrix}
\]

Re-express as: \( \tilde{M} \tilde{v} = \tilde{0} \)

\[
\tilde{M} = 
\begin{pmatrix}
a_{11} & a_{12} \\
a_{21} & a_{22}
\end{pmatrix}, \quad \tilde{v} = 
\begin{pmatrix}
x \\
y
\end{pmatrix}, \quad \tilde{0} = 
\begin{pmatrix}
0 \\
0
\end{pmatrix}
\]
1. 4 Linear algebra review

• Q: What are the solutions?

• A: There is one that is trivial \( \tilde{\nu} = \begin{pmatrix} 0 \\ 0 \end{pmatrix} \)

• Q: Do others exist?

• A: Yes, but the system of equations must be redundant
1. 4 Linear algebra review

- $a_{11} x + a_{12} y = 0 \quad \& \quad a_{21} x + a_{22} y = 0$

- $y = -\frac{a_{11}}{a_{12}} x \quad \& \quad y = -\frac{a_{21}}{a_{22}} x$

- $y = -\frac{a_{11}}{a_{12}} x = -\frac{a_{21}}{a_{22}} x$

- If $x \neq 0$, then $\frac{a_{11}}{a_{12}} = -\frac{a_{21}}{a_{22}}$

- Or: $a_{11}a_{22} - a_{12}a_{21} = 0$
1. 4 Linear algebra review

• This must hold to satisfy our equations simultaneously:
  • \( a_{11}a_{22} - a_{12}a_{21} = 0 \)

• **Q:** Can we reinterpret this result?

• **A:** \( \det(\tilde{M}) = \det\begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix} = a_{11}a_{22} - a_{12}a_{21} \)
1. 4 Linear algebra review

• In order to have a NON-TRIVIAL solution to the system of equations (1), we must have

\[ \det(\tilde{M}) = 0 \]

• Q: Can we apply this to our system of lin eqs?

\[
\begin{align*}
x_{n+1} &= a_{11}x_n + a_{12}y_n \\
y_{n+1} &= a_{21}x_n + a_{22}y_n
\end{align*}
\]
1. 4 Linear algebra review

• **A**: Re-write in matrix/vector notation

\[
\tilde{v}_{n+1} = \tilde{M} \tilde{v}_n \quad \tilde{v}_n = \begin{pmatrix} x_n \\ y_n \end{pmatrix}
\]

• Similar to the one-dimensional case let’s guess that

\[
\tilde{v}_n = \begin{pmatrix} A\lambda^n \\ B\lambda^n \end{pmatrix}, \text{ where } A \text{ and } B \text{ depend on the initial conditions}
\]
1. 4 Linear algebra review

- Now we need to find $\lambda$
- Substitute in:

$$
\begin{pmatrix}
A\lambda^{n+1} \\
B\lambda^{n+1}
\end{pmatrix} = \tilde{M} \begin{pmatrix}
A\lambda^{n} \\
B\lambda^{n}
\end{pmatrix} = \begin{pmatrix}
a_{11} & a_{12} \\
a_{21} & a_{22}
\end{pmatrix} \begin{pmatrix}
A\lambda^{n} \\
B\lambda^{n}
\end{pmatrix}
$$

- $A\lambda^{n+1} = a_{11} A\lambda^{n} + a_{12} B\lambda^{n}$
- $B\lambda^{n+1} = a_{21} A\lambda^{n} + a_{22} B\lambda^{n}$
1. 4 Linear algebra review

• After canceling out $\lambda^n$, we obtain:

• $A \lambda = a_{11} A + a_{12} B$
• $B \lambda = a_{21} A + a_{22} B$

• $A (a_{11} - \lambda) + B a_{12} = 0$
• $A a_{21} + B (a_{22} - \lambda) = 0$
1. 4 Linear algebra review

• Rewrite & reduce the system linear equations to a system of linear algebraic equations:

\[
\begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix} = \begin{pmatrix} a_{11} - \lambda & a_{12} \\ a_{21} & a_{22} - \lambda \end{pmatrix} \begin{pmatrix} A \\ B \end{pmatrix}
\]

• Now we either have the trivial solution:

\[
\begin{pmatrix} A \\ B \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix} \quad \text{OR} \quad \det \begin{pmatrix} a_{11} - \lambda & a_{12} \\ a_{21} & a_{22} - \lambda \end{pmatrix} = 0
\]
1. 4 Linear algebra review

• The zero determinant can be expressed as:
  \[(a_{11} - \lambda)(a_{22} - \lambda) - a_{12} a_{21} = 0\]

• \[\lambda^2 - (a_{11} + a_{22})\lambda + a_{11} a_{22} - a_{12} a_{21} = 0\]

• \[\lambda^2 - \beta \lambda + \gamma = 0\]
• With solutions: \[\lambda_{1,2} = \frac{\beta \pm \sqrt{\beta^2 - 4\gamma}}{2}\]
1. 4 Linear algebra review

Q: what are the values λ

A: the eigenvalues of matrix M

\[ \lambda_{1,2} = \frac{\beta \pm \sqrt{\beta^2 - 4\gamma}}{2} \]

In conclusion, given \( \tilde{v}_{n+1} = \tilde{M} \tilde{v}_{n+1} \), there exist solutions of the form \( \tilde{v}_n = \lambda^n \tilde{v}_0 \), where \( \lambda \) is an eigenvalue of matrix \( \tilde{M} \).
1. 4 Linear algebra review

- **Note:** each eigenvalue has an associate eigenvector:

\[
\tilde{M} \tilde{v}_1 = \lambda_1 \tilde{v}_1 \quad \tilde{M} \tilde{v}_2 = \lambda_2 \tilde{v}_2
\]

- Example: \( \tilde{M} = \begin{pmatrix} 2 & 2 \\ 1/2 & 2 \end{pmatrix} \)

- Compute eigenvalues and eigenvectors
1. 4 Linear algebra review

- Example: $\tilde{M} = \begin{pmatrix} 2 & 2 \\ 1/2 & 2 \end{pmatrix}$

- Compute eigenvalues and eigenvectors

$$\det(\tilde{M} - \lambda I) = \begin{pmatrix} 2 & 2 \\ 1/2 & 2 \end{pmatrix} - \lambda \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} = \begin{pmatrix} 2 - \lambda & 2 \\ 1/2 & 2 - \lambda \end{pmatrix} = 0$$

$$(2 - \lambda)^2 - 1 = \lambda^2 - 4\lambda + 3 = 0 \quad \Rightarrow \lambda_1 = 1, \lambda_2 = 3$$
1. 4 Linear algebra review

• **Q:** What are the eigenvectors?  \( \tilde{M} \tilde{v}_2 = \lambda_2 \tilde{v}_2 \)

• **A:** Write the equations and solve for \( a, b \)

\[
\begin{pmatrix}
2 & 2 \\
1/2 & 2 \\
\end{pmatrix}
\begin{pmatrix}
a \\
b \\
\end{pmatrix}
= 3
\begin{pmatrix}
a \\
b \\
\end{pmatrix}
\]

\[
2a + 2b = 3a, \quad \Rightarrow 2b = a
\]

\[
\frac{1}{2}a + 2b = 3b, \quad \Rightarrow 1/2a = b
\]

Redundant, just choose \( a = 2, b = 1 \)
1. 4 Linear algebra review

- **Q:** What are the eigenvectors? \( \tilde{M} \tilde{v}_1 = \lambda_1 \tilde{v}_1 \)
- **A:** Write the equations and solve for \( a, b \)

\[
\begin{pmatrix}
  2 & 2 \\
  1/2 & 2
\end{pmatrix}
\begin{pmatrix}
  a \\
  b
\end{pmatrix}
= 1
\begin{pmatrix}
  a \\
  b
\end{pmatrix}
\]

\[
2a + 2b = a, \quad \Rightarrow -2b = a
\]

\[
\frac{1}{2}a + 2b = b, \quad \Rightarrow 1/2a = -b
\]

Redundant, just choose \( a = -2, b = 1 \)
1. 4 Linear algebra review

- In summary M has the following eigenvectors and eigenvalues:

<table>
<thead>
<tr>
<th></th>
<th>Eigenvalues</th>
<th>Eigenvectors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$\lambda_1 = 1$</td>
<td>$\begin{pmatrix} 2 \ 1 \end{pmatrix}$</td>
</tr>
<tr>
<td>2</td>
<td>$\lambda_2 = 3$</td>
<td>$\begin{pmatrix} -2 \ 1 \end{pmatrix}$</td>
</tr>
</tbody>
</table>
1. 4 Linear algebra review

- Graphical representation

- Any vector in the plane is a linear combination of the eigenvectors

\[
\tilde{x} = \begin{pmatrix} x \\ y \end{pmatrix} = c_1 \tilde{v}_1 + c_2 \tilde{v}_2; \quad c_1 = c_2 = 1/2
\]
1. 4 Linear algebra review

- E. g. \( \tilde{x} = \begin{pmatrix} 0 \\ 1 \end{pmatrix} \Rightarrow \begin{pmatrix} 0 \\ 1 \end{pmatrix} = c_1 \begin{pmatrix} 2 \\ 1 \end{pmatrix} + c_2 \begin{pmatrix} -2 \\ 1 \end{pmatrix} \)

- \( 0 = 2c_1 - 2c_2 \Rightarrow c_1 = c_2 \)

- \( 1 = c_1 + c_2, \quad 1 = 2c_1 \Rightarrow c_1 = c_2 = \frac{1}{2} \)

- Check: \( \frac{1}{2} \begin{pmatrix} 2 \\ 1 \end{pmatrix} + \frac{1}{2} \begin{pmatrix} -2 \\ 1 \end{pmatrix} = \begin{pmatrix} 0 \\ 1 \end{pmatrix} \)
1. 4 Linear algebra review

• Matlab code:

• \([\text{eigenvalues, eigenvectors}] = \text{eigs}([2 2; 1/2 2])\)

• \(\text{eigenvalues} =\)
  \[
  0.8944 \quad -0.8944 \\
  0.4472 \quad 0.4472
  \]

• \(\text{eigenvectors} =\)
  \[
  3 \quad 0 \\
  0 \quad 1
  \]
1. 4 Linear algebra review

• **Q:** Why is this useful?

• **A:** Remember \( \tilde{\nu}_{n+1} = \tilde{M}\tilde{\nu}_n \)

• To solve, one needs to compute the eigenvectors and eigenvalues for matrix M
1. 4 Linear algebra review

• Then, given initial conditions we can write

\[ \tilde{v}_0 = C_1 \tilde{v}_- + C_2 \tilde{v}_+ \]

\[ \tilde{v}_1 = \tilde{M} \tilde{v}_0 = \tilde{M} \left( C_1 \tilde{v}_- + C_2 \tilde{v}_+ \right) = \]

\[ C_1 \tilde{M} \tilde{v}_- + C_2 \tilde{M} \tilde{v}_+ = C_1 \lambda_1 \tilde{v}_- + C_2 \lambda_2 \tilde{v}_+ \]
1. 4 Linear algebra review

• For the second iteration:

\[ \tilde{v}_2 = \tilde{M} \tilde{v}_2 = \tilde{M} (C_1 \lambda_1 \tilde{v}_- + C_2 \lambda_2 \tilde{v}_+) = \]

\[ C_1 \lambda_1 \tilde{M} \tilde{v}_- + C_2 \lambda_2 \tilde{M} \tilde{v}_+ = C_1 \lambda_1^2 \tilde{v}_- + C_2 \lambda_2^2 \tilde{v}_+ \]

• By induction:

\[ \tilde{v}_n = C_1 \lambda_1^n \tilde{v}_- + C_2 \lambda_2^n \tilde{v}_+ \]
1. 4 Linear algebra review

• **Q:** Will the solution grow/decay?
• **A:** Depends on the specific eigenvalues.

• E. g. $1 < \lambda_1 < \lambda_2$. Let $n \to \infty$

$$\tilde{v}_n = C_1 \lambda_1^n \tilde{v}_- + C_2 \lambda_2^n \tilde{v}_+ =$$

$$\lambda_2^n (C_1 \left( \frac{\lambda_1}{\lambda_2} \right)^n / \lambda_2^n \tilde{v}_- + C_2 \tilde{v}_+) \approx C_2 \lambda_2^n \tilde{v}_+$$
1. 4 Linear algebra review

- Remember the system of equations:
  \[ R_{n+1} = (1 - f) \, R_n + M_n \]
  \[ M_{n+1} = \gamma \, f \, R_n \]

- Assume that one of the eigenvectors is \( \tilde{v}_+ = \begin{pmatrix} 2 \\ 1 \end{pmatrix} \)

\[
\begin{pmatrix} R_n \\ M_n \end{pmatrix} = \tilde{v}_n \approx C_2 \lambda_2^n \tilde{v}_+ = C_2 \lambda_2^n \begin{pmatrix} 2 \\ 1 \end{pmatrix}
\]

- Then \( R_n/M_n = 2/1 = 1 \), that is, fixed ratio
1. 4 Linear algebra review

• E. g. $0 < \lambda_1 < \lambda_2 < 1$. Let $n \to \infty$

$$\tilde{v}_n = C_1 \lambda_1^n \tilde{v}_- + C_2 \lambda_2^n \tilde{v}_+ \to 0$$

• In general if magnitude of both is less than 1, solutions decay

• If at least the magnitude of at least one eigenvalues is more than 1 it explodes
Red blood cell example revisited

- \( R_{n+1} = (1 - f) R_n + M_n \)
- \( M_{n+1} = \gamma f R_n \)

- Use linear algebra instead of combining the equations

\[
\begin{pmatrix}
  R_{n+1} \\
  M_{n+1}
\end{pmatrix}
= \begin{pmatrix}
  1 - f & 1 \\
  \gamma f & 0
\end{pmatrix}
\begin{pmatrix}
  R_n \\
  M_n
\end{pmatrix}
= \tilde{A}
\begin{pmatrix}
  R_n \\
  M_n
\end{pmatrix}
\]
Red blood cell example revisited

• **Q:** What are the eigenvalues of matrix $A$?

• **A:** compute the determinant

$$
\begin{vmatrix}
1 - f - \lambda & 1 \\
\gamma f & -\lambda \\
\end{vmatrix} = 0
$$

• $(1 - f - \lambda)(-\lambda) - \gamma f = 0$

• $\lambda^2 - \lambda (f - 1) + \gamma f = 0$
Red blood cell example revisited

• Approach 1 and 2 yield identical results

\[ \lambda_{1,2} = \frac{1 - f \pm \sqrt{(1 - f)^2 + 4 \gamma f}}{2} \]

• Can the # RBC be constant in the future?
• Under what conditions?
Red blood cell example revisited

• The larger eigenvalue is 1

\[ 1 = \frac{1 - f \pm \sqrt{(1 - f)^2 + 4\gamma f}}{2} \]

\[ 1 + f = \sqrt{(1 - f)^2 + 4\gamma f} \]

\[ 1 + 2f + f^2 = 1 - 2f + f^2 + 4\gamma f \]

• True if \( \gamma = 1 \)
Red blood cell example revisited

• Easy to check that:

• $\lambda_1 = -f$, $\lambda_2 = 1$

• $f$ is the fraction of RBC remove ($0 < f < 1$)

• Remember that solution are on the form:

$$\tilde{v}_n = C_1 \lambda_1^n \tilde{v}_- + C_2 \lambda_2^n \tilde{v}_+$$
Red blood cell example revisited

• It is easy to see now that:

\[
\tilde{v}_n = C_1 \lambda_1^n \tilde{v}_- + C_2 \lambda_2^n \tilde{v}_+ = C_1 1^n \tilde{v}_- + C_2 (-f)^n \tilde{v}_+ \approx C_1 \tilde{v}_-
\]

• The resultant state is now constant, and depends only on the initial conditions
Red blood cell example revisited

• Stable solutions requires $\gamma = 1$

• It is true that our body is tuned so that the number of RBC produced in the marrow per day is the same lost in the spine (so that $\gamma = 1$)?
  • Probably not

• What happens in $\gamma < 1$, or $\gamma > 1$