Calculating Biological Quantities

CSCI 2897

Prof. Daniel Larremore

daniel.larremore@colorado.edu
@danlarremore

2021, Lecture 2

Lecture 2 Plan

1. **One minute review of the basics:**
    1. Website
    2. Syllabus
    3. Canvas
    4. Slack
2. **Office Hours?**
3. **Asking “modeling” questions**
4. **Some vocabulary**
5. **Steps to modeling a biological problem (1-4)**

Last Time on CBQ…

Sean Taylor
FB Research

- Website: https://github.com/dblarremore/CSCI2897
    - Homework & reading posted, Code examples, Class notes
- Syllabus: https://github.com/dblarremore/CSCI2897#syllabus
- Canvas: Turn in homework, Lecture links, Check grades
- Slack: **Didn't get the invite? Stick around after class—we'll get you set up!**
- Textbook: See Slack.

like
this
PDF

Office Hours?

① Post a link → book 15 min slots.

② Drop-in. Set hours. Show up. I'll be on Zoom.

↓

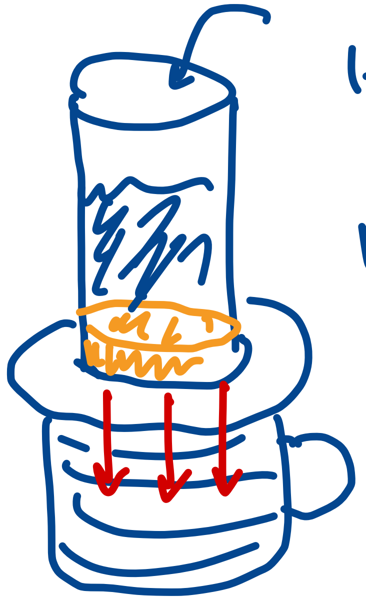
Mix of both, why not.

Dynamical Models 101: Ask a question

Easily rephrased as dynamical models.

- Think about a problem that puzzles you. changes over time
- Draw a "flow diagram" that illustrates the various processes at work.
- *Dynamical* models describe how a system changes over time.

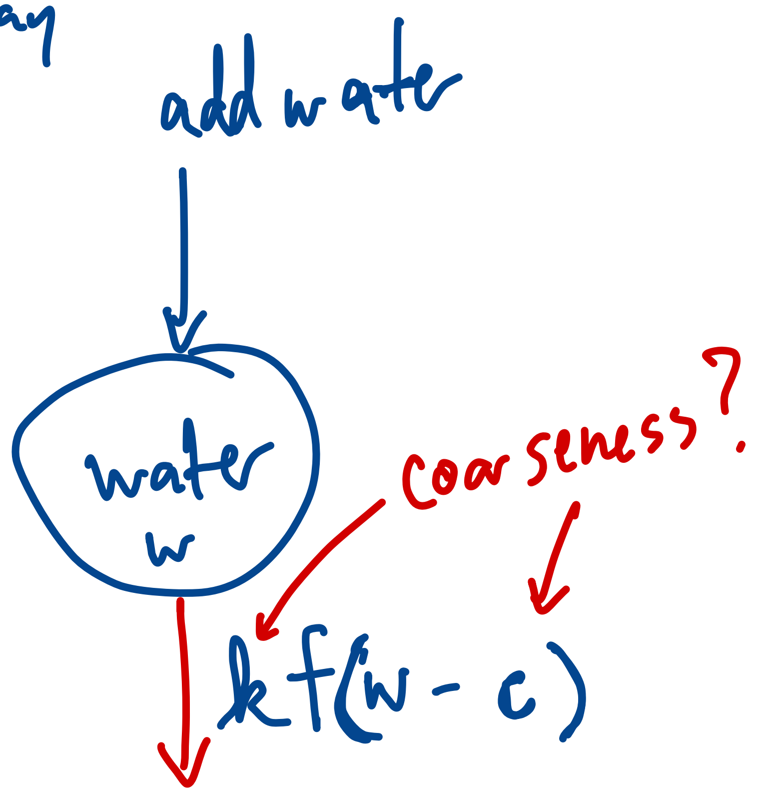
① Aeropress — makes coffee.



If I fill to top.
↓
water drops to middle.

If I fill it ½ way
↓
water doesn't percolate.

What determines the Δ in the water in aeropress over time?



Examples

② How does heat/oil affect how much of the egg is burned?

③ How long does it take for the soil in my plant to dry out? (T, time since watering last, sun, humidity)

Deterministic vs Stochastic dynamical models

this course

- **Deterministic** models assume that the future is entirely predicted (i.e. determined) by the model.

Q: How much H_2O is in my coffee maker?

Model: Flow in / Flow out → deterministic.

- **Stochastic** models assume that random (stochastic) events affect the system.

Q: How much snow at Eldora? (base height?)

Model: Stochastic · snow fall,
· temperature

include a random variable
(source of that stochasticity)

Otto & Day: 7 steps to modeling a biological problem

1. Formulate the question

- What do you want to know?
- Describe that in the form of a question.
- Boil the question down.
- Start with the simplest, biologically reasonable description of the problem.

story.

"Explain it like I'm 5"

Otto & Day: 7 steps to modeling a biological problem

1. Formulate the question
2. Determine the basic ingredients

Define: - variables
- constraints?
- interaction among variables.

Decide: time as discrete vs continuous?

time scale. $t=0$ vs $t=1$ ... day? year? season? second?

Define: - parameters
- constraints
  - fundamental
  - reasonable

Q: what's the diff? parameter vs. variable?

fixed

change over time

mathy stuff
autonomous vs. non-autonomous
Diff. Eqns

preview!

Otto & Day: 7 steps to modeling a biological problem

1. Formulate the question
2. Determine the basic ingredients
3. Qualitatively describe the biological system

Life cycle diagrams

Flow diagrams

Event tables

Otto & Day: 7 steps to modeling a biological problem

LHS — lefthand side
RHS — righthand side.

1. Formulate the question
2. Determine the basic ingredients
3. Qualitatively describe the biological system
4. Quantitatively describe the biological system

Diagrams (guide) $\longrightarrow$ Equations

Checks: • constraints hold?
• units on LHS vs RHS of equations

Big: Can the model <u>actually</u> answer Q in step 1?

Otto & Day: 7 steps to modeling a biological problem

1. Formulate the question
2. Determine the basic ingredients
3. Qualitatively describe the biological system
4. Quantitatively describe the biological system
5. Analyze the equations

- solve (analytical)
- simulate (numerical)
- analyze

Math class

APPM
Diff. Eq.

Otto & Day: 7 steps to modeling a biological problem

1. Formulate the question
2. Determine the basic ingredients
3. Qualitatively describe the biological system
4. Quantitatively describe the biological system
5. Analyze the equations
6. Checks & balances

- check against known examples. e.g. if I don't water for 1 year → soil is v. dry.
- generalizability?
- alternatives to your model? (reflecting? repeating prev. steps)

Otto & Day: 7 steps to modeling a biological problem

1. Formulate the question
2. Determine the basic ingredients
3. Qualitatively describe the biological system
4. Quantitatively describe the biological system
5. Analyze the equations
6. Checks & balances
7. Relate the results back to the question

- Did your model help answer the Q?
- Intuitive? Counterintuitive?
- Tell a story to summarize the model. Insights?
- Experiments?

1. Formulate the question

- Find a living / biological object/thing /stuff
- Ask a Q about how it might Δ over time?

Delta (capital) change

δ (lowercase delta)

1. How does # branches on a tree change over time?
2. How does a cat change the # of mice in a barn?
3. How does # people w/ COVID change over a year?

pop. growth

immigration

interactions among variables

you can tell what the variable is!

2. Determine the basic ingredients

- **Variables**: what entities might change over time?
- Assign a letter to each variable. (Hint: use “intuitive” letters!)
- Write down *fundamental* constraints on your variables.
- Write down *reasonable* constraints on your variables.

notes:

- $n(t)$ explicitly saying "of t"
- alternatives:
  - n_t, n_{t+1}
  - n (no t)

\# branches $\quad n(t) \geq 0$

\# mice $\quad n(t) \geq 0$

\# infected ppl. $\quad I(t) \geq 0$

\# recovered $\quad R(t) \geq 0$

\# susceptible $\quad S(t) \geq 0$

$I(t) + R(t) + S(t) =$ pop. size

conventions:

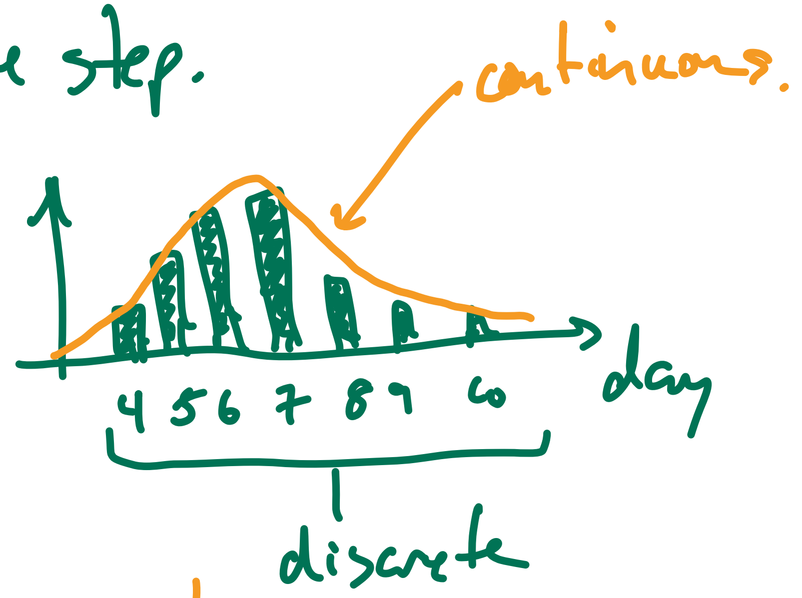
$n = \#$

$p =$ proportion

$\left.\begin{matrix} n_1(t) \\ n_2(t) \end{matrix}\right]$ two species

Discrete time vs Continuous time

- **Discrete time models**: "jumpy"
  - assume that Δs cannot compound within a time step.
  - ↑ holds well if Δt is small/reasonable
  - Ex: viral load in SARS-CoV-2 infections



- **Continuous time models**: "smooth"
  - Assumes that variables can change at any point in time!
  - Seems better?

    But: could be unrealistic! Ex: You may need to grow to a certain size before branching.

- **Note:**

  Sometimes math is easier one way vs another!

Be clear about your time scale

- **Discrete time models**:
  - COVID models : day
  - Animal Pops over longer time : season/year
  - Soil Moisture : hours

  "tick" of the clock

- **Continuous time models**:
  - How long has passed between $t=1$ and $t=0$?

btw…

- You'll have to decide whether your variables are discrete or continuous too!

branches: integer ≥ 0
mice: integer ≥ 0
discrete.

$\mathbb{R}$ = real #s.

↓

biomass mice: $\mathbb{R} \geq 0$

Infectious Diseases:

S I R

→ integers ≥ 0 (people)

→ $0 \leq \mathbb{R} \leq 1$ (pop. proportions)

btw…

- You'll have to decide whether your variables are discrete or continuous too!

(1) Often, values get large enough that you can model a discretized population as continuous (with little error).

(2) Sometimes you can reinterpret a variable to go discrete → cont. (# mice → mouse biomass)

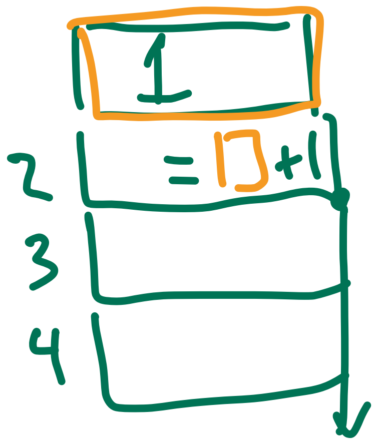
(3) Easier Math

Recursion Equations

- A **recursion equation** describes the value of a variable in the next time step.

  $n(t+1) =$ "some function of $n(t)$"

- Examples.

- 

  Excel

- Bank Balance

Dynamic?

- Conversion to binary (?)

- Fibonacci

  $n(t+1) = n(t) + n(t-1)$

note: "second order"

Difference Equations

- A **difference equation** describes the difference between a variable's values in two successive time steps

$$\Delta n = n(t+1) - n(t) = \text{"some function of } n(t)\text{"}$$

definition

- Examples.

• Excel: $\Delta n = 1$

interest rate

• Bank Interest: $\Delta x = r\, x(t)$

Differential Equations

Q: $\frac{dx(t)}{dt} = r\,x(t) + b\,x(t-1)$

delay diff. equation. tough!

- A **differential equation** describes the rate of change of the variable over time

$$\frac{dn(t)}{dt} = \text{"some function of } n(t)\text{"}$$

- Examples.

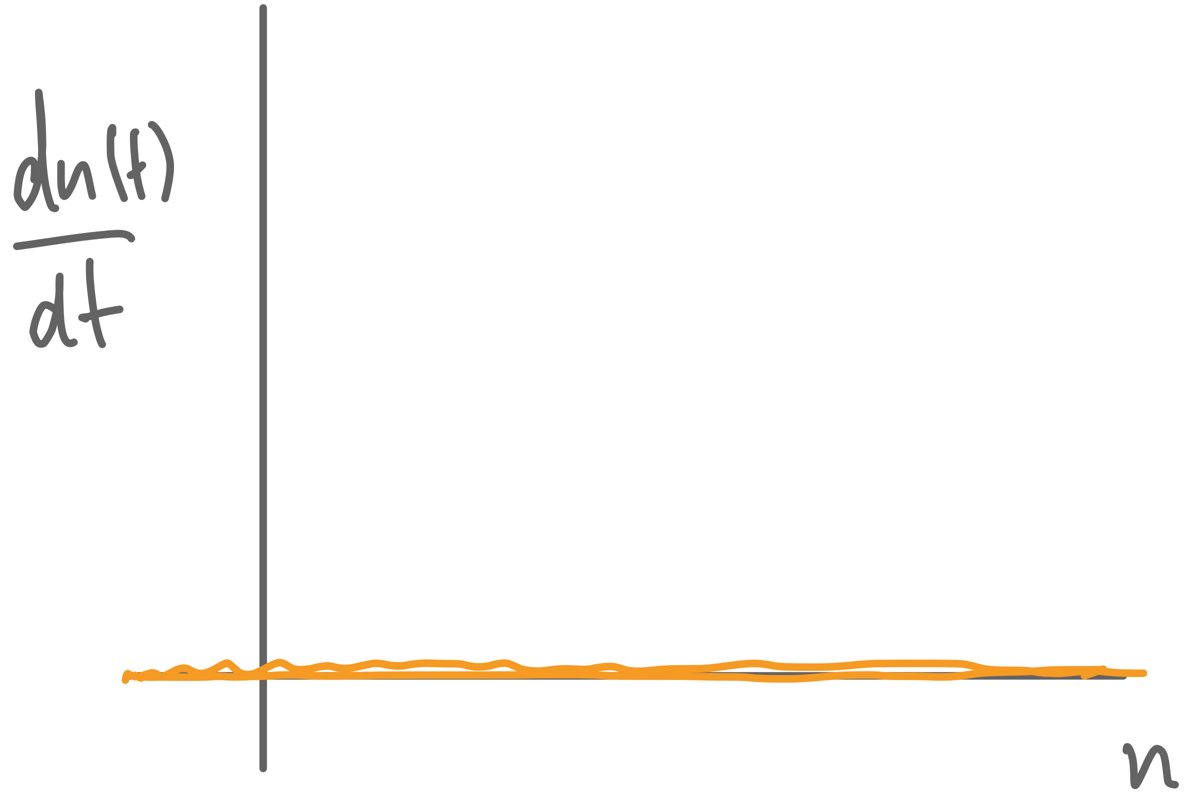
• Interest $\quad \frac{dn(t)}{dt} = r\,n(t)$

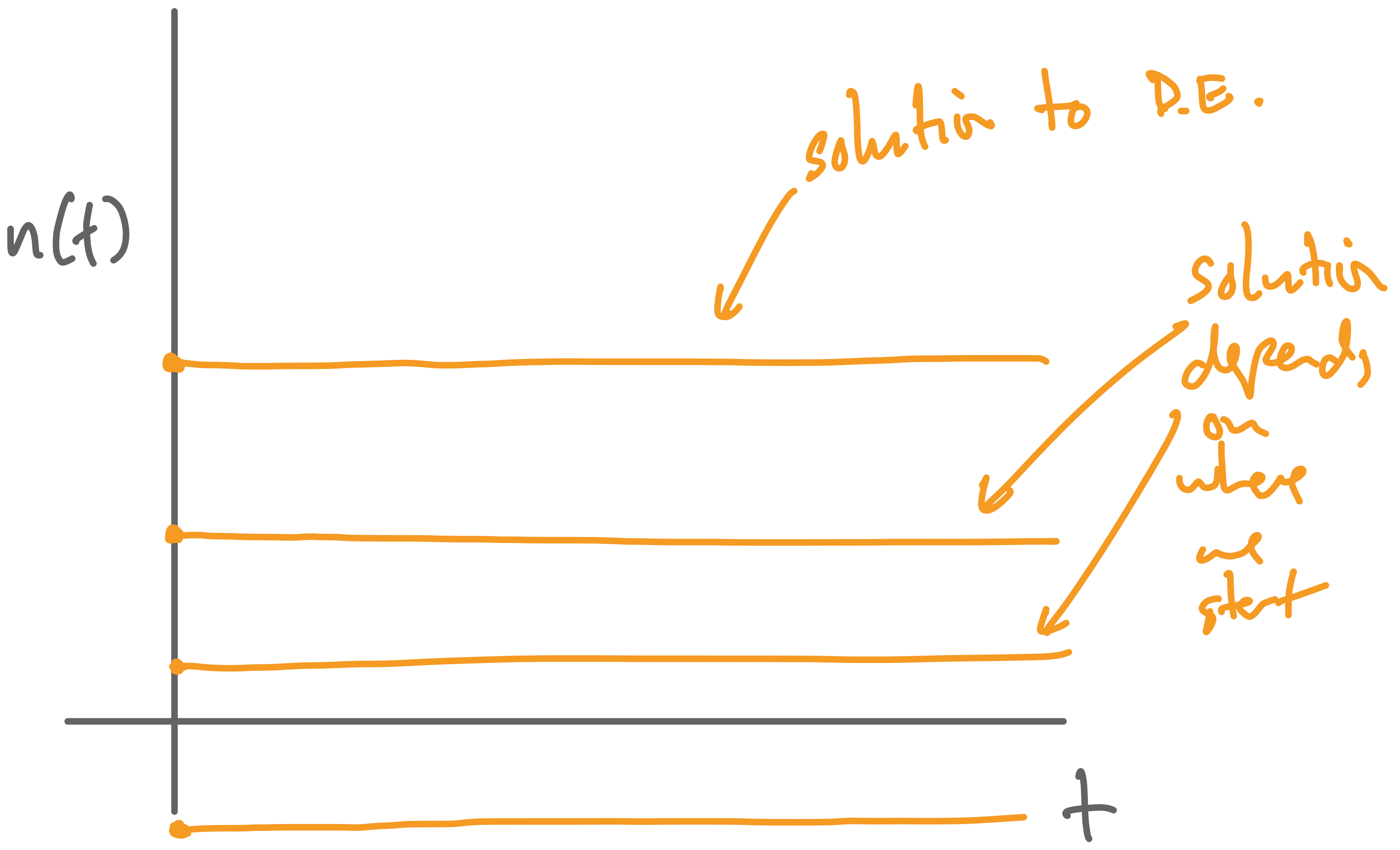
• Newton's Law of Cooling $\quad \frac{dT(t)}{dt} = -k\left(T(t) - T_{room}\right)$

Examples for Intuition

- Ex 1: (A) Sketch the derivative vs ~~time~~ n. (B) Sketch the variable vs time.

$$\frac{dn(t)}{dt} = 0$$

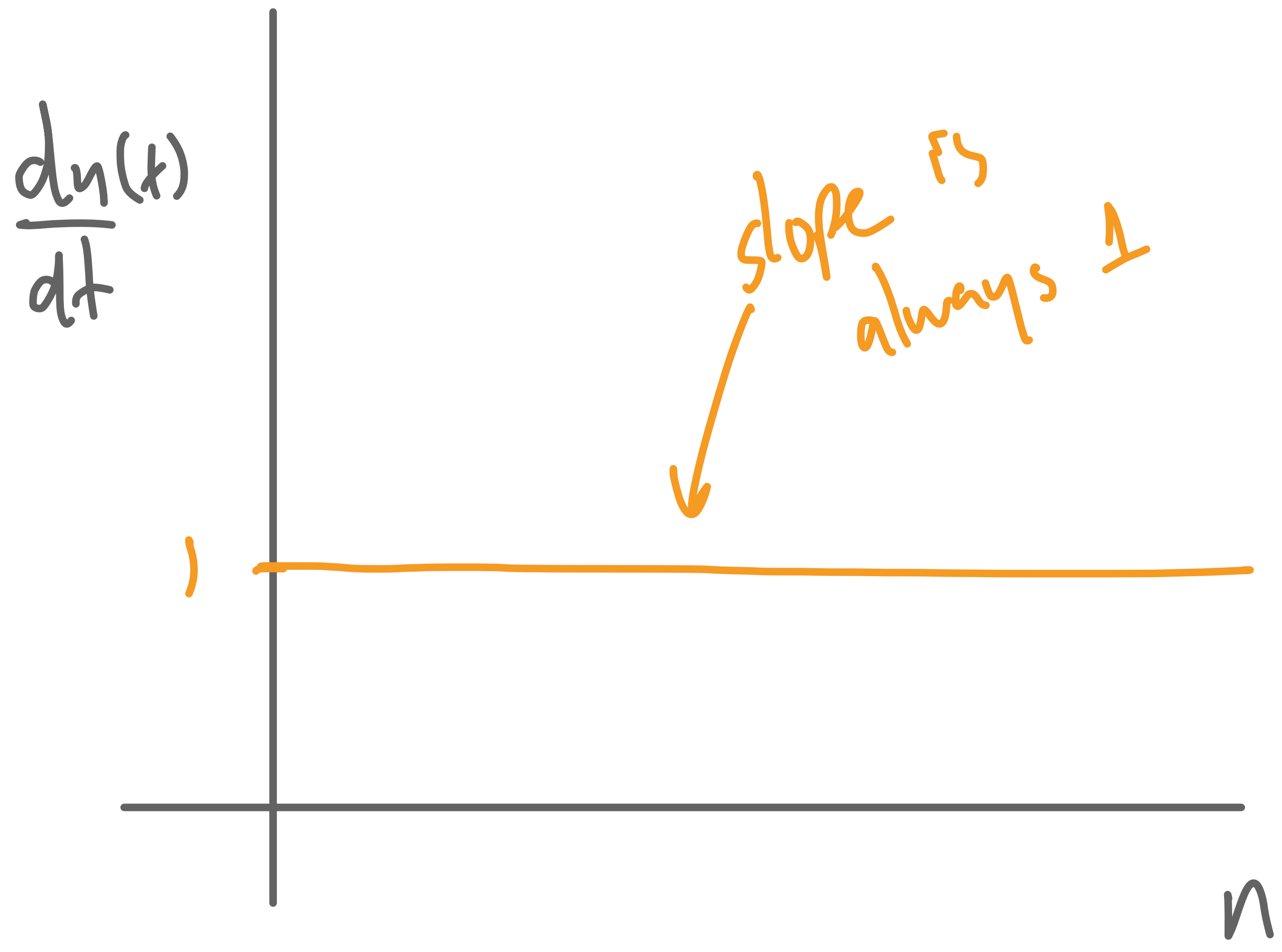


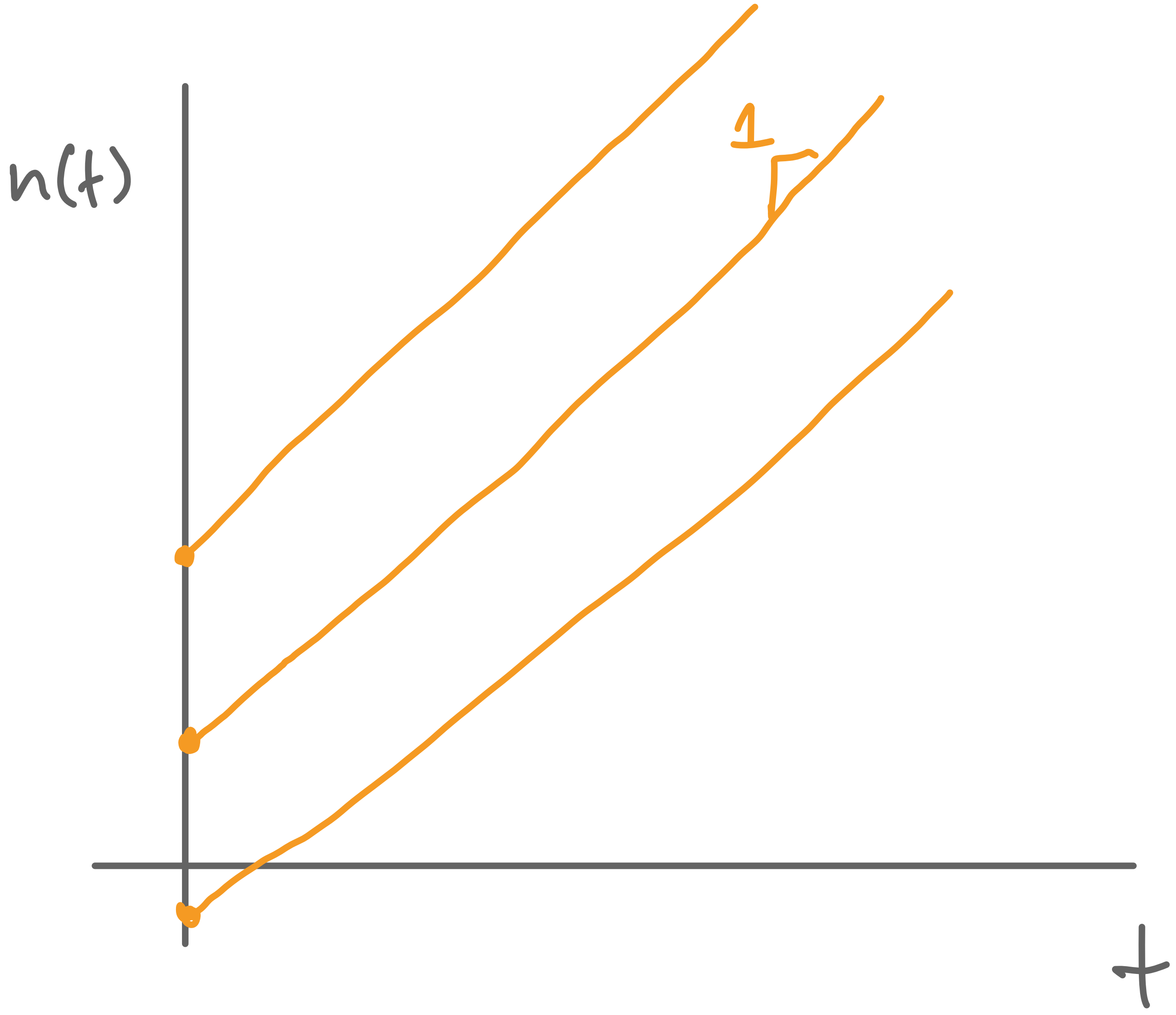


Examples for Intuition

- Ex 2: (A) Sketch the derivative vs ~~time~~ n. (B) Sketch the variable vs time.

$$\frac{dn(t)}{dt} = 1$$

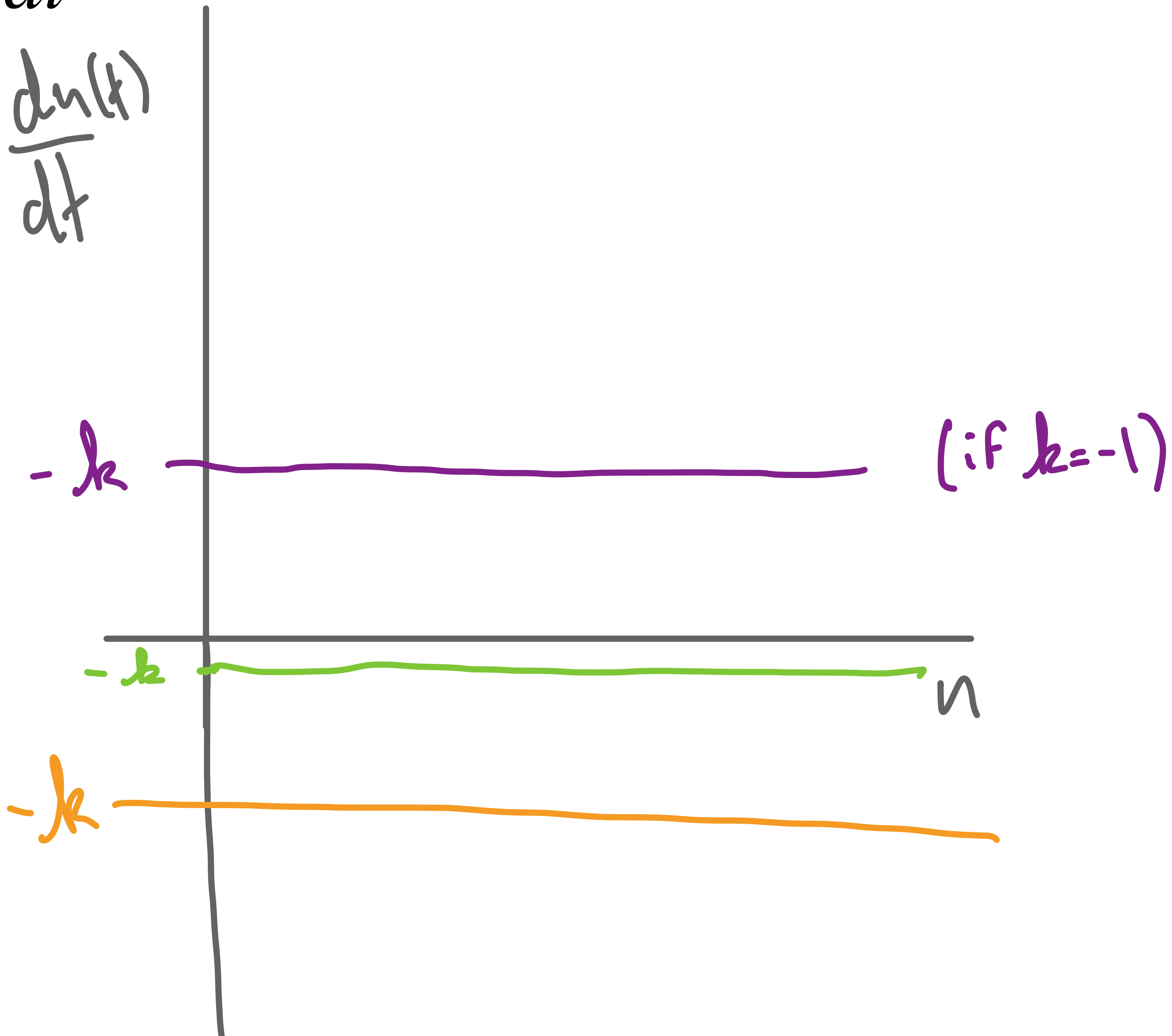


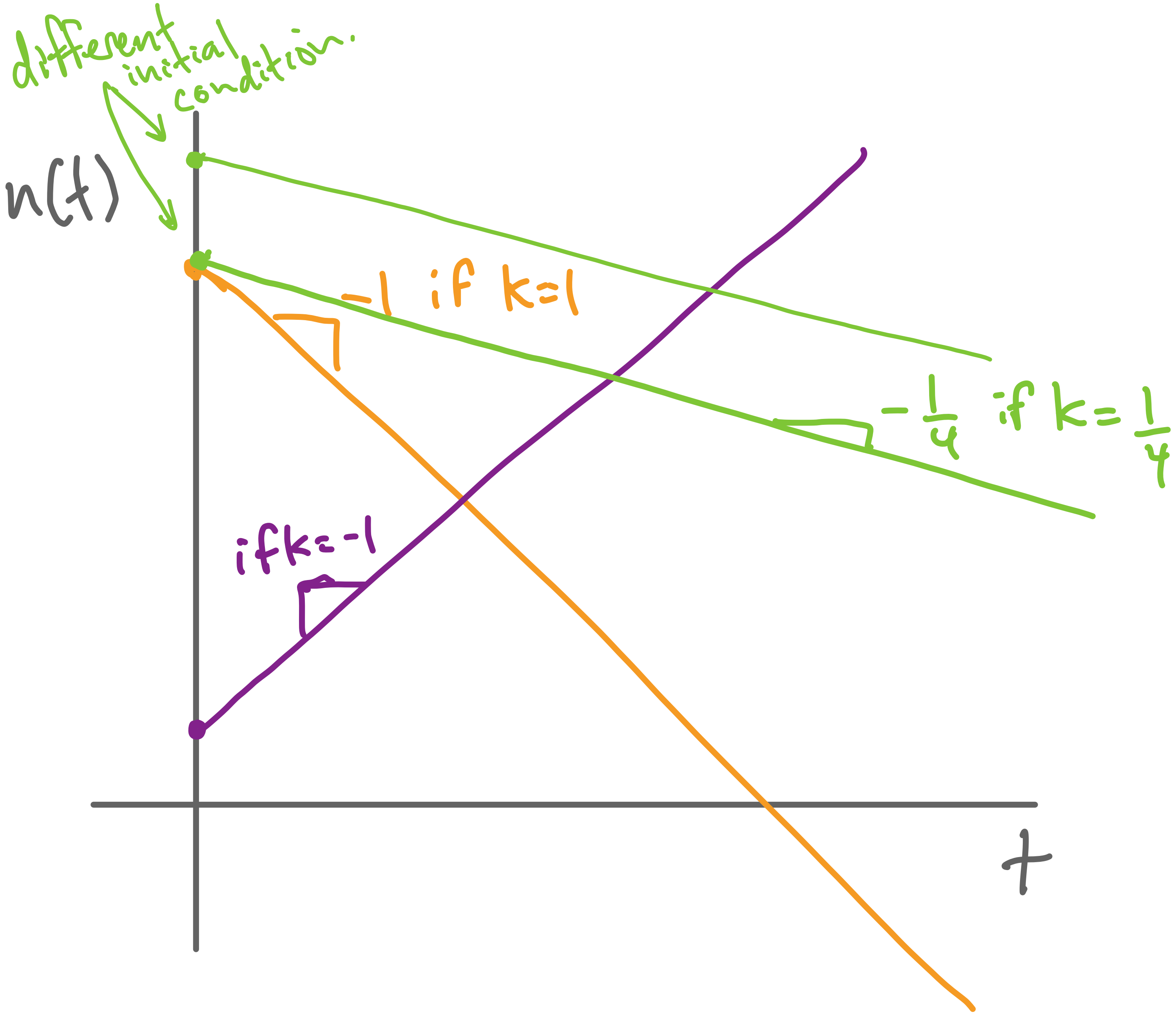


Examples for Intuition

- Ex 3: (A) Sketch the derivative vs ~~time~~ n. (B) Sketch the variable vs time.

$$\frac{dn(t)}{dt} = -k$$





Examples for Intuition

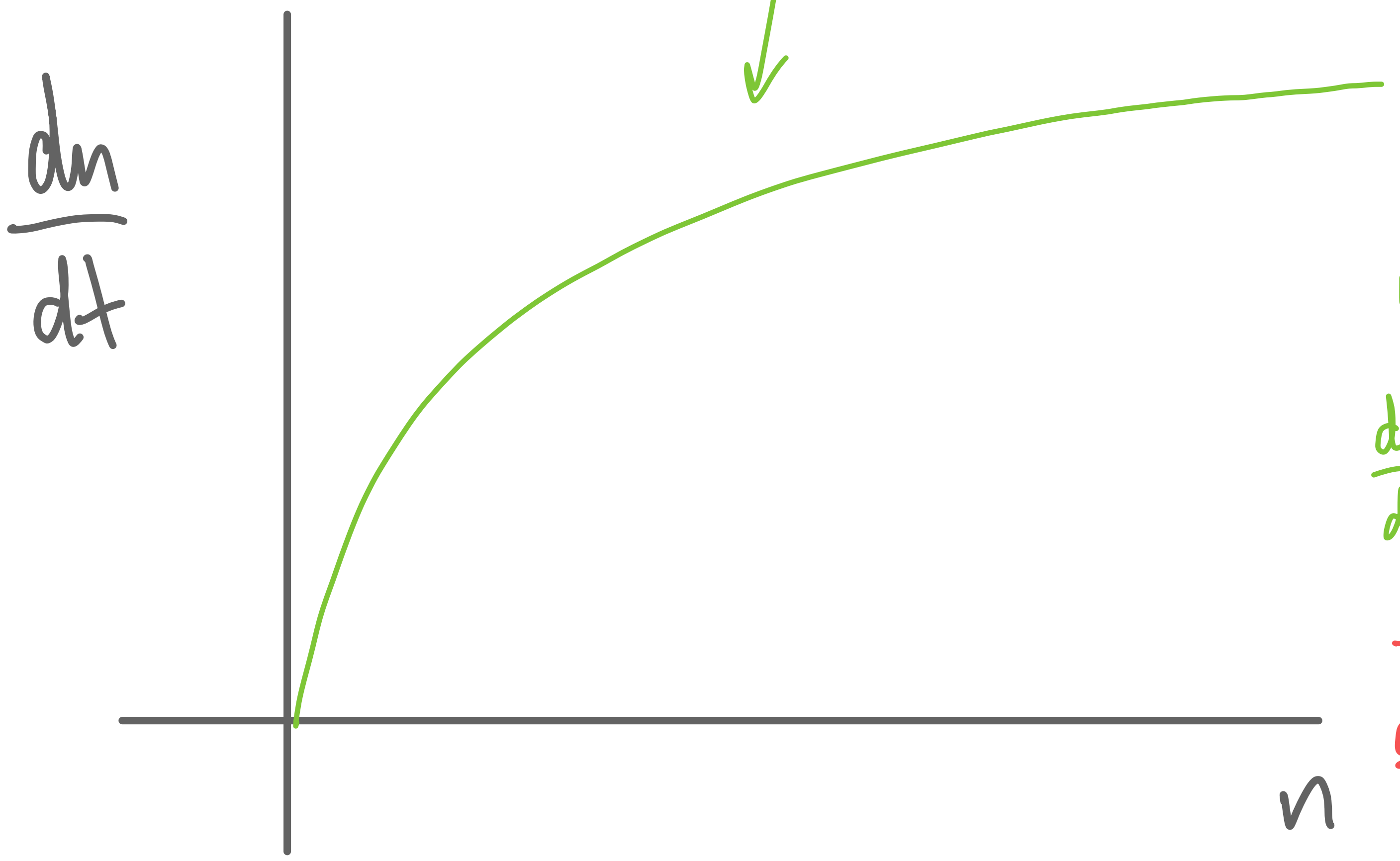
"numerical solution"

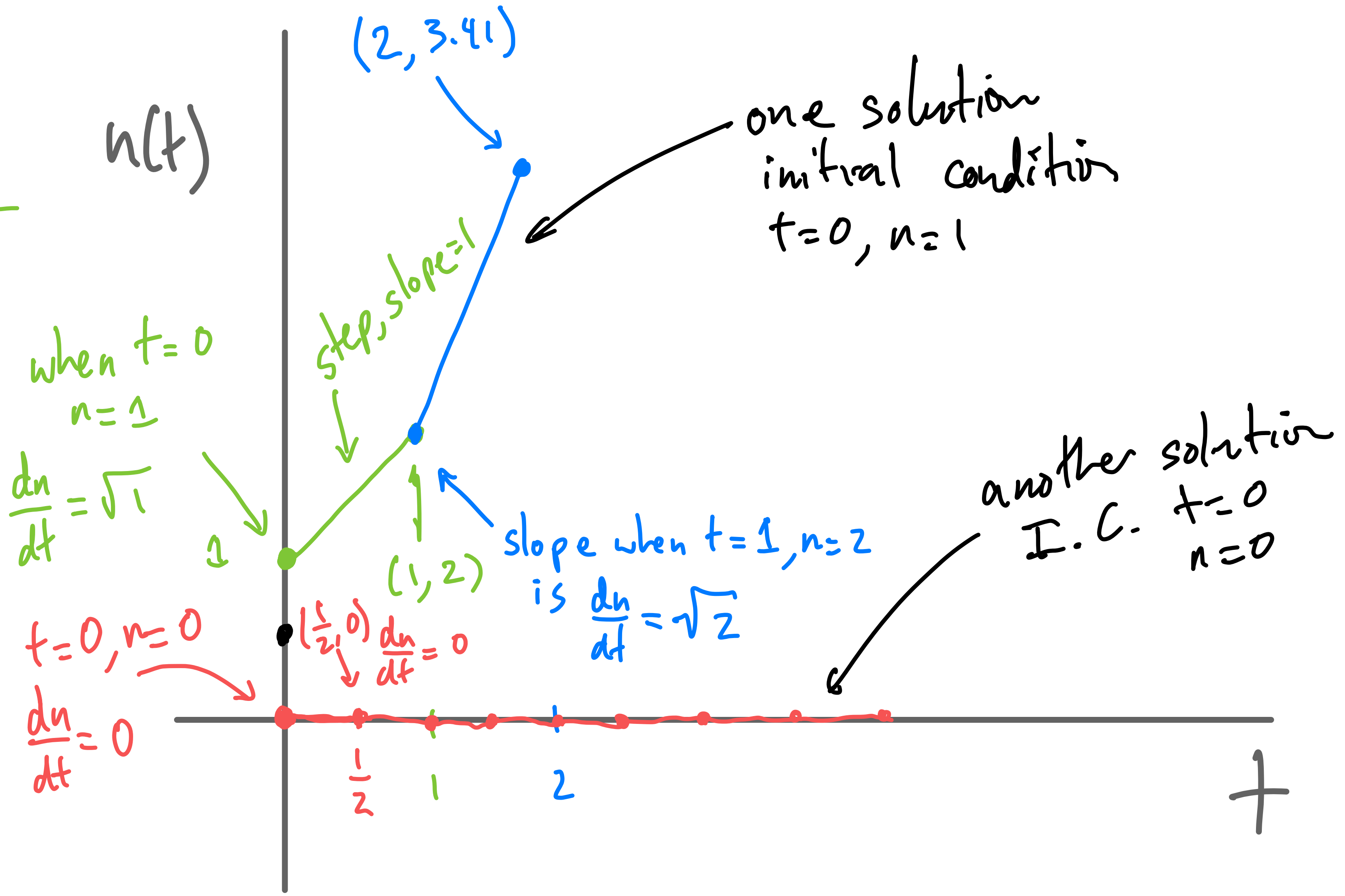
$y = 3*x$
LaTeX/MarkDown

- Ex 4: (A) Sketch the derivative vs time. (B) Sketch the variable vs time.

$$\frac{dn(t)}{dt} = \sqrt{n}$$

typical "$\sqrt{x}$"





slope $= \sqrt{n}$ → What function (of t) has a slope of $\sqrt{n(t)}$

Parameters

- The **parameters** of the model are quantities that influence the dynamics but remain fixed over time.
- Examples:

$$\frac{dn}{dt} = -k$$

Interest: $n(t+1) = r\,n(t) + n(t)$

$$\frac{dn}{dt} = r\,n(t)$$

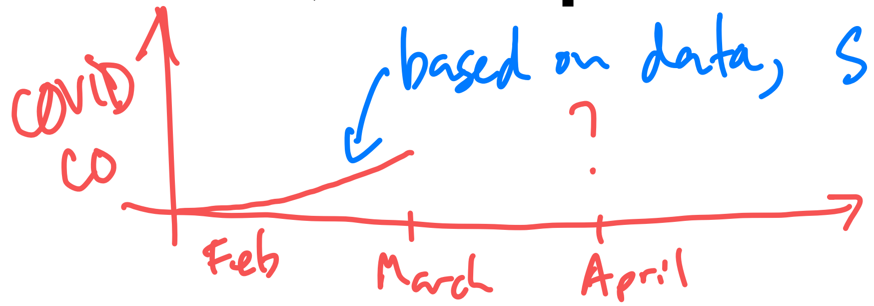
- Branches per day per existing branch b
- Fraction of mice eaten by cat per day death d
- # mice born, per day, per mouse birth b
- Fraction of healthy exposed to infected people per day c
- Prob. of transmission per exposure a

Parameters

See $\frac{dn}{dt} = \sqrt{n}$ slide.

- The **parameters** of the model are quantities that influence the dynamics but remain fixed over time.
- When we fix parameters and look at a trajectory of the equation, that's called **forward simulation** or **forward integration**. Model + Parameters → Data
- When we have data and a model, and we determine the values of the parameters that best fit the data, that's **parameter inference.** Model + Data → Parameters

e.g.



based on data, SEIR model for disease, what are the spreading parameters?

- Note: parameters' units need to match the kind of model we're using.
- Note: parameters may have *reasonable* ranges in addition to *fundamental* ranges.

it would be surprising/weird if $r = 100\%$

Interest rate $r \geq 0$

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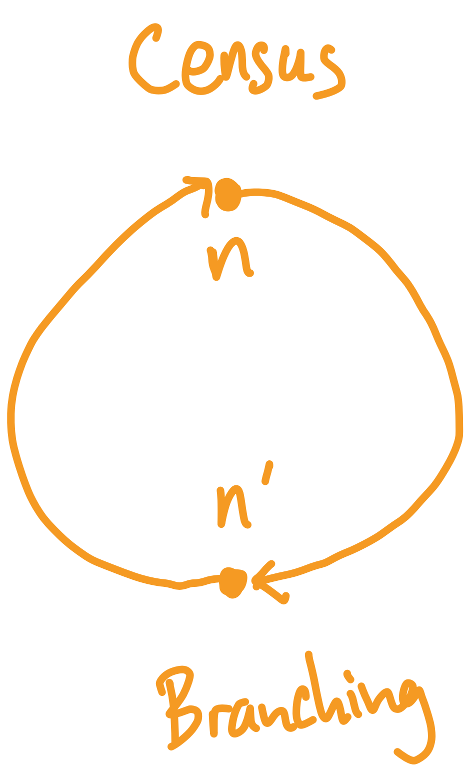
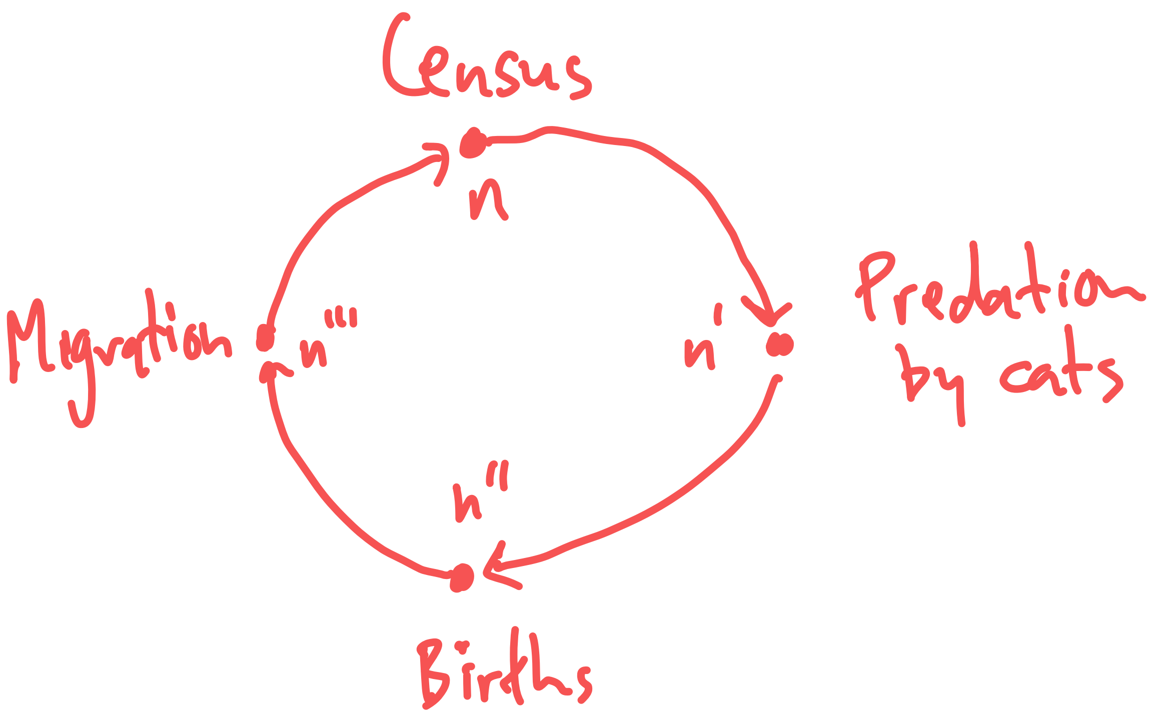
Diagrams: Life Cycle

- Keep track of the events occurring during a single time step *and their order*.

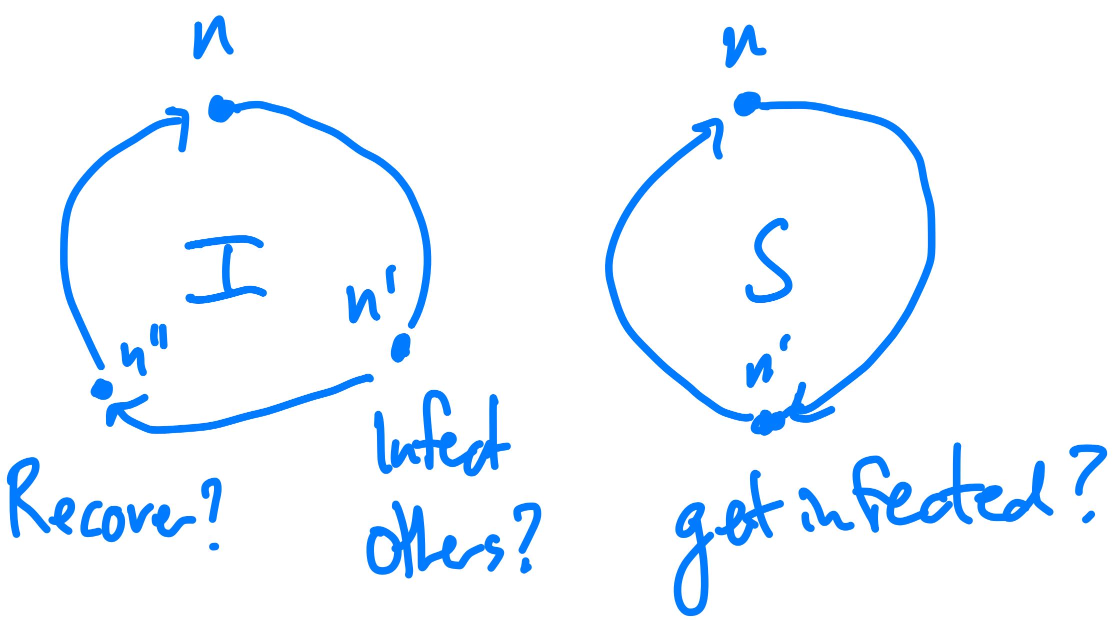
Tree Branches



Mice in Yard



COVID



Order matters.

Census → Cats → Births → Migration.

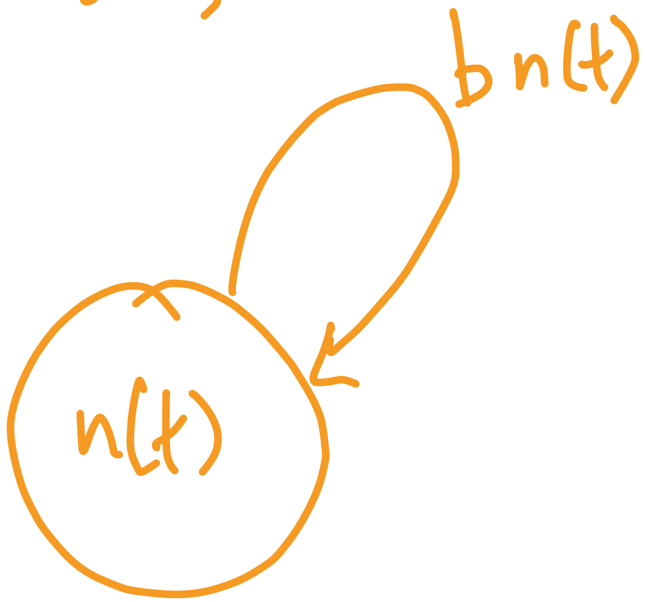
Track multiple variables

I, S

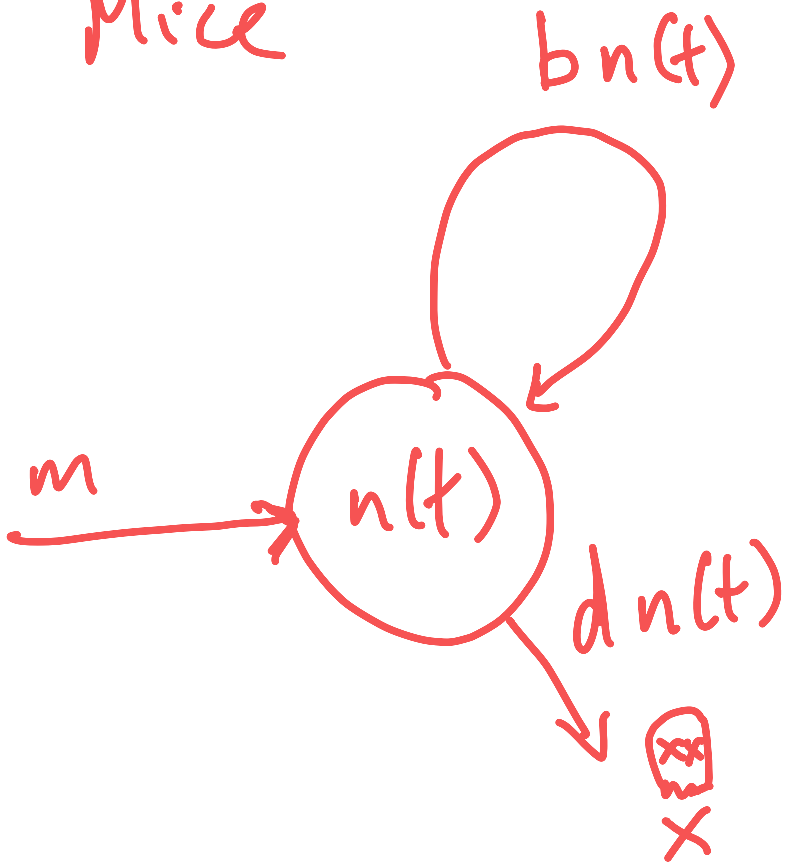
Diagrams: Flow

- Keep track of the events occurring during a single time step *and their order*.

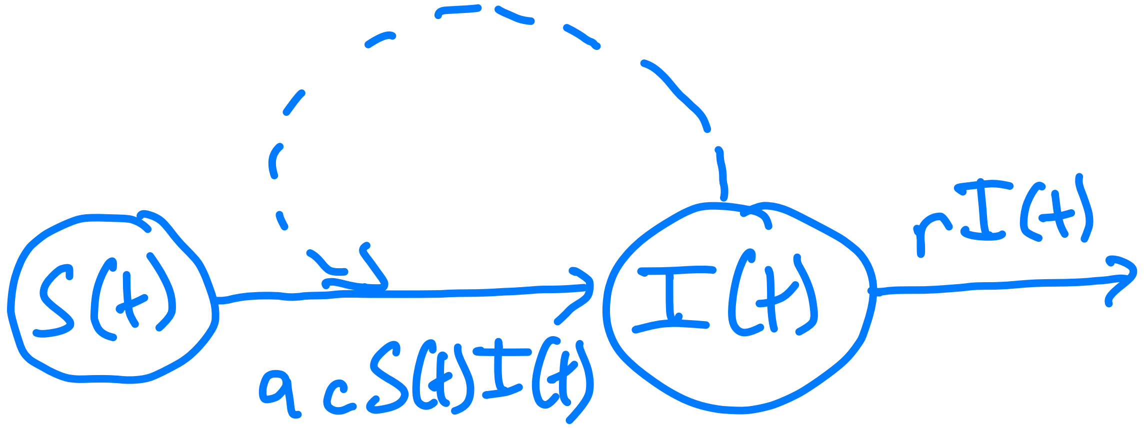
Branches



Mice



COVID



Multiple Variables

Diagrams: Table of Events

- Discrete-time models with **multiple events** per time step and **multiple variables**.

Interaction	# events	Result of Event: I	Result of Event: S
$I \times I$	$c\,I(t)\,I(t)$	$-$	$-$
$S \times S$	$c\,S(t)\,S(t)$	$-$	$-$
$I \times S$	$c\,S(t)\,I(t)$	$+a$	$-a$

law of mass action

Pros and Cons?

- See Otto & Day, Chapter 2.4

Otto & Day: 7 steps to modeling a biological problem

✓1. Formulate the question
✓2. Determine the basic ingredients
✓3. Qualitatively describe the biological system
4. Quantitatively describe the biological system
5. Analyze the equations
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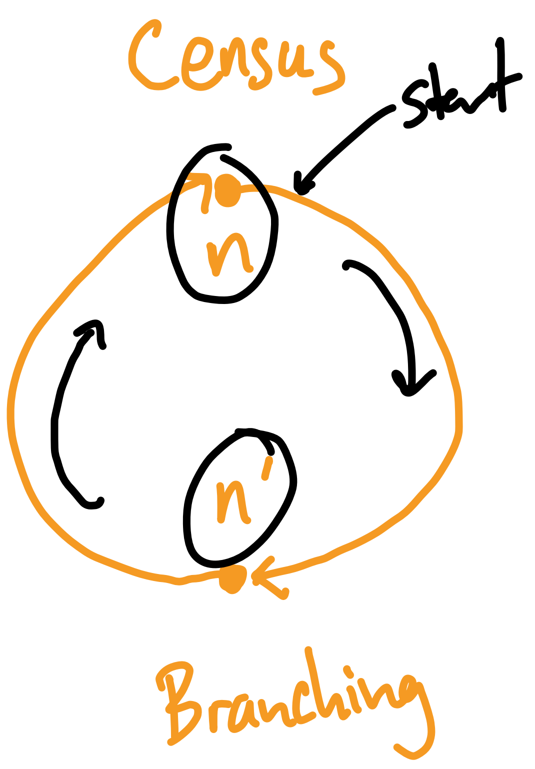
7. Relate the results back to the question

Example: tree branching

note: b is a parameter <u>not</u> a function of t.

- Use the life cycle diagram to derive a recursion, and use that to create a difference equation.

Tree Branches



$$n'(t) = n(t) + b\,n(t)$$

$$n(t+1) = n'(t)$$

$$n(t+1) = n(t) + b\,n(t)$$

$$\boxed{n(t+1) = (1+b)\,n(t)}$$

$$\Delta n = n(t+1) - n(t)$$

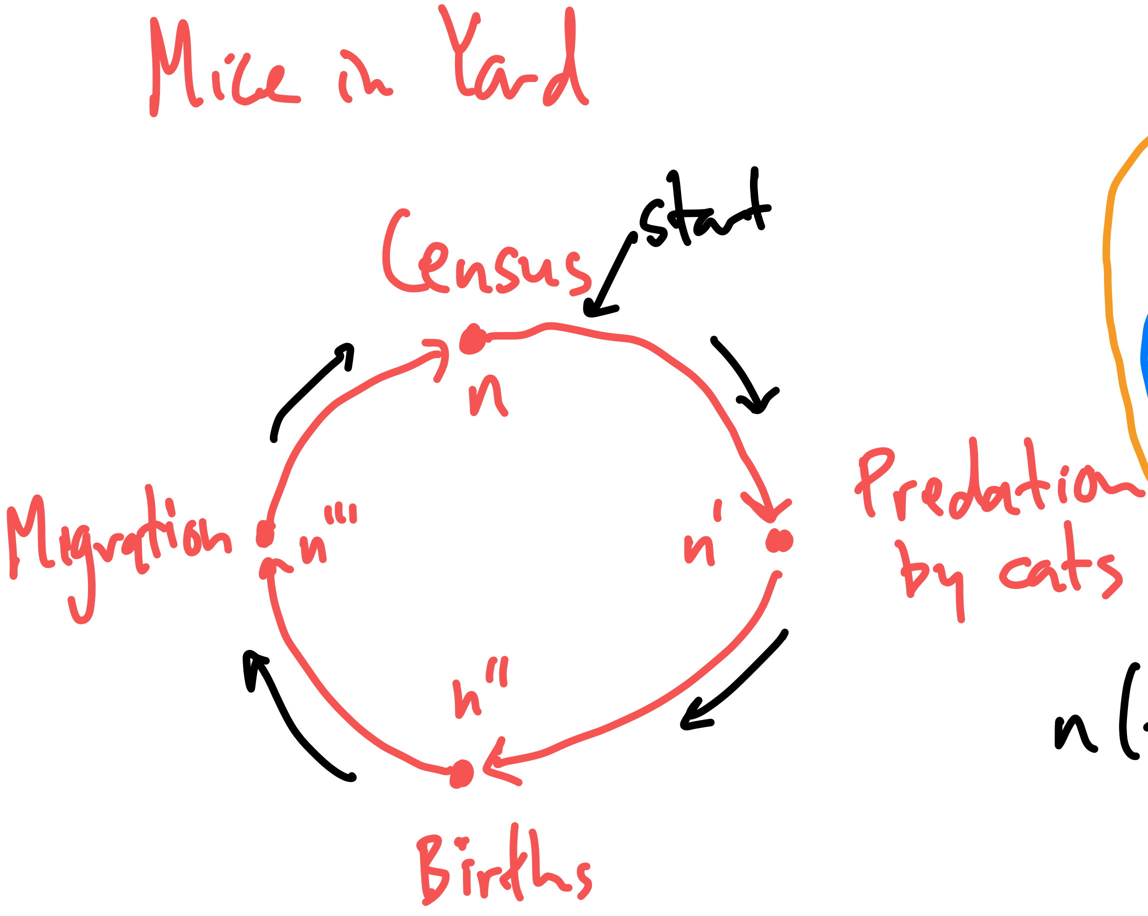
$$\Delta n = (1+b)\,n(t) - n(t)$$

$$\Delta n = \cancel{n(t)} + b\,n(t) - \cancel{n(t)}$$

$$\boxed{\Delta n = b\,n(t)}$$

Example: mouse model

- Use the life cycle diagram to derive the stages of the recursion.



$$n'(t) = n(t) - d\,n(t)$$

$$n''(t) = n'(t) + b\,n'(t)$$

$$n'''(t) = n''(t) + m$$

$$\begin{aligned} n(t+1) &= n'''(t) \\ &= n''(t) + m \\ &= \left[n'(t) + b\,n'(t)\right] + m \end{aligned}$$

$$\boxed{n(t+1) = (1+b)\left[n(t) - d\,n(t)\right] + m}$$

same

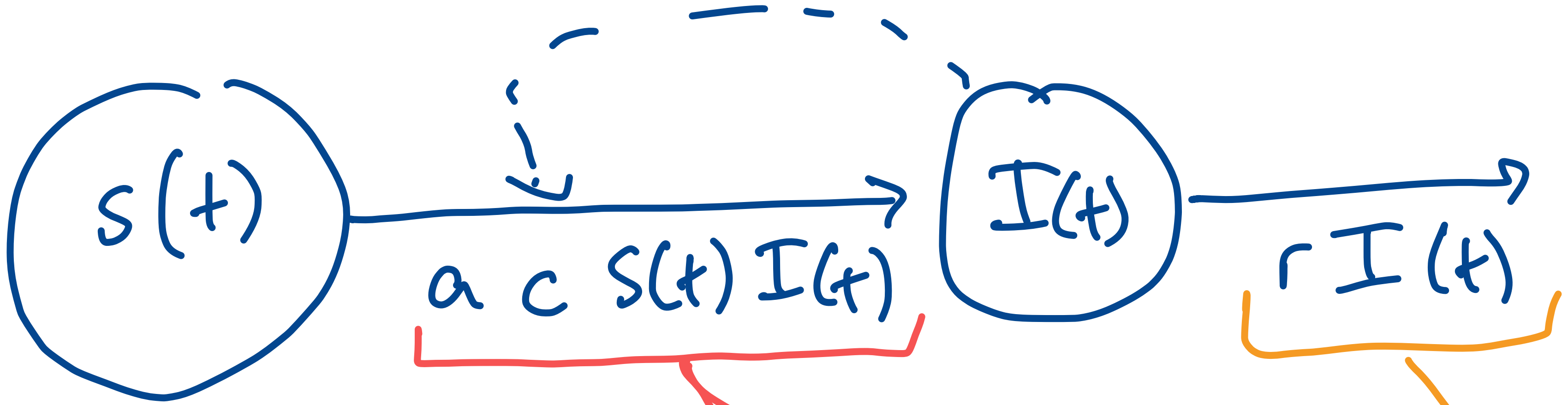
$$\boxed{n(t+1) = (1+b)(1-d)\,n(t) + m}$$

Recipes: recursion & difference equations from life cycle diagrams

1. Use $n'(t), n''(t), n'''(t)$ etc to denote the variable's value after each life cycle event.
2. Set $n(t+1)$ to the value of n after the final event in the cycle.
3. Substitute, and get $n(t+1)$ in terms of $n(t)$ by eliminating $n'(t)$ etc.
4. optional Subtract $n(t)$ from both sides and simplify to get the difference equation
   $\Delta n = n(t+1) - n(t) = \dots$

Example: COVID-19

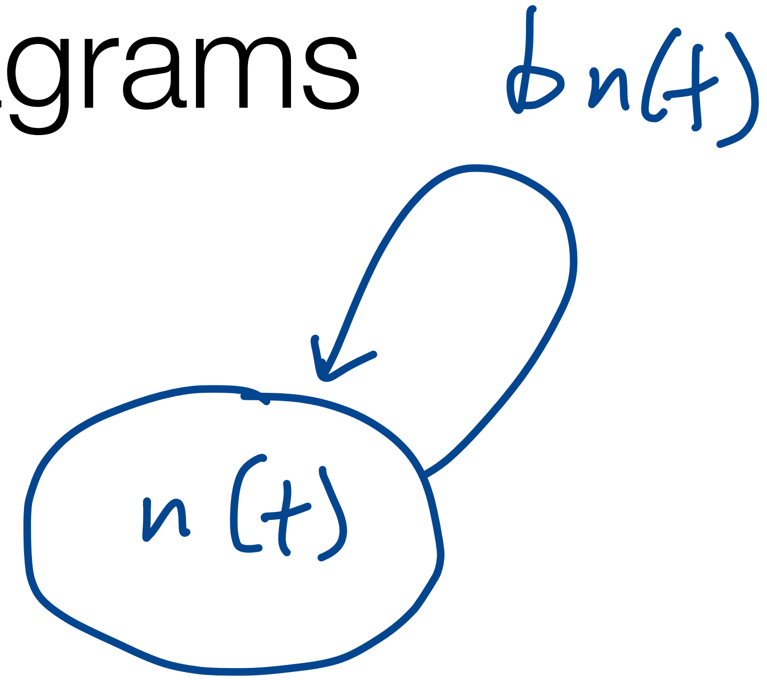
- Use the flow diagram to create the recursion equations for COVID-19 spread.



$$S(t+1) = S(t) - a\,c\,S(t)\,I(t)$$

$$I(t+1) = I(t) + a\,c\,S(t)\,I(t) - r\,I(t)$$

Recipes: differential equations from flow diagrams



$$\frac{d(n(t))}{dt} = \ldots$$

the flow rates along arrows *entering* the circle

+ the flow rates along arrows leaving & returning to the circle

– the flow rates along arrows exiting the circle

$$\frac{dn}{dt} = bn(t)$$

rate of change only

$$n(t+1) = n(t) + bn(t)$$

previous value

amount of change

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