Life Sciences Outreach Fall Faculty Speaker Series
Teacher Professional Development Activity
Modeling and Game Theory

THE DEREK BOK CENTER FOR TEACHING AND LEARNING
HARVARD

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Overview

This activity was designed for an audience of classroom high school biology teachers as part of a professional development program to further their knowledge in a research field. It has not been formally formatted or tested for a high school student audience because we believe that teachers are the best interpreters of content for their students. Therefore, we welcome teachers to adapt this activity for their own classroom needs.

Objective

The purpose of this activity is to show how integration of mathematical and computational modeling approaches can be used to help better understand cooperation and conflict in microbial communities. In particular, we will focus on integration of genome-scale models of metabolism and evolutionary game theory to study interactions between "cheater" and "cooperator" strains of yeast (*Saccharomyces cerevisiae)*. We also will demonstrate how principles of game theory apply to human interactions.

References

Zomorrodi A, Segrè D. Genome-driven evolutionary game theory helps understand the rise of metabolic interdependencies in microbial communities. 2017. Nature Communications: 8(1563). https://doi.org/10.1038/s41467-017-01407-5

Morgan SN, Sharp MD, Grogan KA. So You Want to Run a Classroom Experiment Online? The Good, the Bad, and the Different. 2020. Applied Economics Teaching Resources: 2(5). https://www.aaea.org/UserFiles/file/AETR_2020_028RRProofFinal-issue_v2.pdf

Activity

Part 1: Game Theory Social Experiment

Background

Game theory is a powerful mathematical modeling framework to study interactions among different agents (players), where the payoff (net benefit) of each player is not only a function of its own strategy but also of other players' strategies. We are going to explore how these theoretical concepts apply to real world phenomena.

Activity

First, we will demonstrate how principles from game theory can be used to understand human interactions. We will split everyone randomly into six firms: Facebook and Twitter, Uber and Lyft, Microsoft and Apple. We will assign a CEO of each firm, who will have the final word in the decision made by their firm over the course of the experiment.

The game will last for three short rounds, each of which represents a year of time in the experiment. At the beginning of each year, each firm will meet in a breakout room and decide to either **compete** or **cooperate** over the price of a major product, the goal being to maximize earnings in each round of the game. The payoffs for competing or colluding are different for each pair of competing companies.

For **Facebook (Group 1)** and **Twitter (Group 2)**, If both decide to compete, each takes home $2 billion. If both cooperate, each takes home $5 billion. But if they choose opposing strategies, the competitor profits $10 billion while the cooperator profits nothing.

For **Uber (Group 3)** and **Lyft (Group 4)**, If both decide to compete, each takes home $0 billion. If both cooperate, each takes home $5 billion. But if they choose opposing strategies, the competitor profits $10 billion while the cooperator profits $5 billion.

For **Apple (Group 5)** and **Microsoft (Group 6)**, If both decide to compete, each takes home $5 billion. If both cooperate, each takes home $10 billion. But if they choose opposing strategies, the cooperator profits $10 billion while the competitor profits nothing.

The CEO should write the decision of the firm on a sheet of paper. We will come back to the main room after each round and ask the CEOs of opposing companies to simultaneously share their decisions, and we'll tabulate the payoffs below.

	Facebook	Twitter	Uber	Lyft	Microsoft	Apple
Round 1						
Round 2						
Round 3						

Discussion

The three situations presented here correspond to three different kinds of "mathematical games." A mathematical game models interactions among rational decision-makers. Here, each firm played a game where the strategies were defined by the payoff values associated with cheating or colluding. We have names to describe the different games that the competing firms played, which we will define later. As (hopefully) rational firms, you collectively chose an outcome that corresponded to your selfish best interest. If you did act rationally, your strategy corresponded to the so-called "Nash equilibrium" strategy. Note that for some games, it is **not** the case that the best overall outcome is the most rational one.

Facebook v. Twitter:

The Nash equilibrium (rational strategy) occurs when each firm competes. Why? They each stand to gain more, as both are guaranteed at least some profit when competing. If one cooperates, they run the risk of taking home no profit whatsoever on the product, even if there is a small chance that they take home the largest amount.

Uber v. Lyft:

The Nash equilibrium (rational strategy) occurs when one firm competes and the other cooperates. Why? In the case that both compete, nobody wins. Everybody wins something when both cooperate, but both firms stand to win even more when taking opposite strategies.

Microsoft v. Apple:

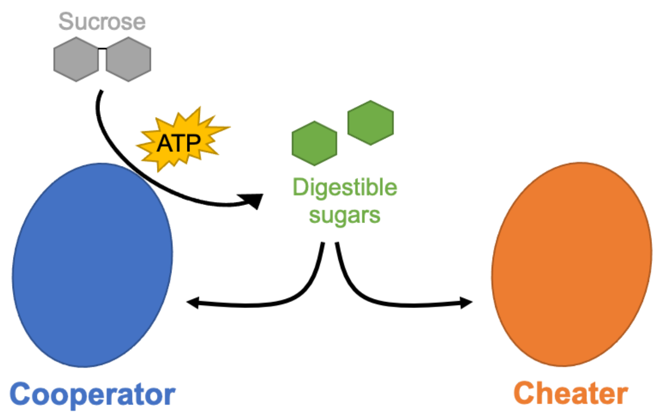
The Nash equilibrium occurs when both firms decide to cooperate. This decision isn't very hard to make—it also happens to be the one that generates the most profit overall!

Though this scenario described the behavior of rational human agents competing for survival in the market, we'll see later how it can be adapted to model the interactions of microbes competing for survival.

Part 2: Game Theory and Metabolic Modeling in Microbial Cooperation and Conflict

Background

We will now be applying some of the same principles of game theory that we have just explored in our social experiment in a biological context. We will be examining evolutionary game theory, the application of game theory to mixed evolving populations in biology. Here, the reproductive fitness of each player is determined by the strategies and frequencies of all players. In addition, we will be exploring how we can combine evolutionary game theory with computational models of biological processes to gain a better understanding of the complex interactions between microbial players in biological settings. More specifically we will be integrating evolutionary game theory with models of metabolism that reflect all of the metabolic reactions occurring in an organism.



Our example system consists of cheater and cooperator strains of the Baker's yeast *Saccharomyces cerevisiae*. In this system, a mixture of cheater and cooperator microbes are grown on a medium where sucrose is the only source of sugar for survival. **Cooperators** (which are wild-type yeast strains) process **sucrose** into more easily **digestible sugars (glucose and fructose)**. This process is energetically costly and requires **ATP**. Some of the digestible sugars produced are retained by the cooperator cell, while the remainder of the sugars leak out into the common space and can be taken up by other microbes. **Cheaters** are mutant yeast strains that cannot process sucrose because their gene for sucrose degradation has been mutated; consequently, they rely on the simple sugars produced by cooperator cells in order to survive.

Note that this yeast system is different from the scenario with the six companies we played at the start of the session. Unlike the human agents who are able to rationally choose whether they want to compete or cooperate, whether or not a given yeast cell cheats or cooperates is genetically determined and cannot change (i.e., one is always a cooperator and the other is always a cheater).

Using our knowledge of evolutionary game theory, we can simulate the interactions between cheaters and cooperators in different conditions and track how the abundance of cheaters and cooperators in the microbial community evolves over time. The outcome of interactions between cheaters and cooperators in this system depends on some key factors:

1. **ATP Coefficient**: the cost of cooperation, that is the amount of energy (ATP) needed to process sucrose. Lower ATP coefficients favor cooperators, and higher ATP coefficients favor cheaters.
2. **Capture Efficiency**: the percentage of digestible sugar retained by cooperators. Whatever the cooperator doesn't keep is released into the environment and will be available for nearby microbes to consume. The higher the capture efficiency, the better for cooperators growth and the worse for cheaters growth.
3. **Fraction Cooperator:** the initial proportion of cooperators in the population. The remaining proportion are cheaters. If the fraction of cooperators is 0.8, then there will be 80% cooperators and 20% cheaters

at time = 0. The fraction of cooperators present in the population at the beginning of the simulation will also impact the outcome.

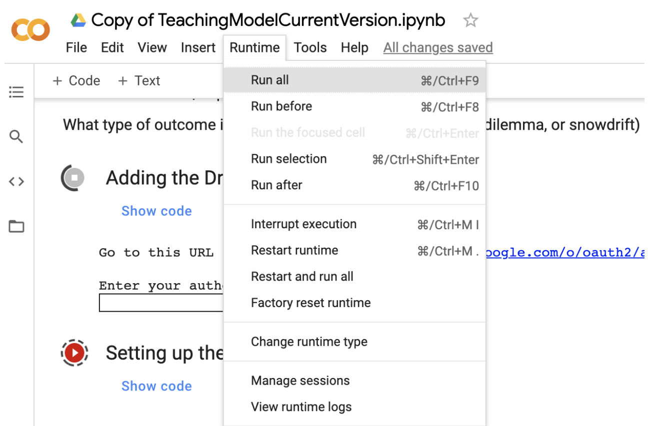
There are three possible outcomes for an evolutionary dynamics model:

1. **Mutually Beneficial Game**: Cooperators dominate, while cheaters go extinct.
2. **Prisoner's Dilemma Game**: Cheaters dominate, while cooperators go extinct.
3. **Snowdrift Game**: A stable equilibrium is established where both cheaters and cooperators co-exist at a certain fraction.

Activity

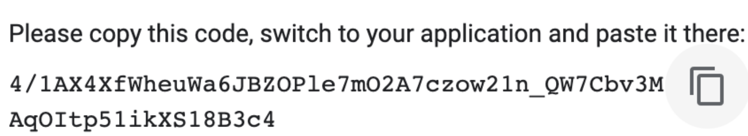
1. Follow this link to the Google Colab document where we will run the simulation: https://colab.research.google.com/drive/1MCKrIgpCu0FcievTdhDP8adHcHrC-xTs?usp=sharing

2. Instructions for running the code for our simulation:
   a. Click the **Runtime button** from the top left and then press **Run all**.



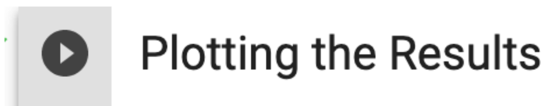
   b. In the first cell, you will be prompted to link to your drive. Click on that link and sign into your Google account.

   Copy the authorization code that appears.



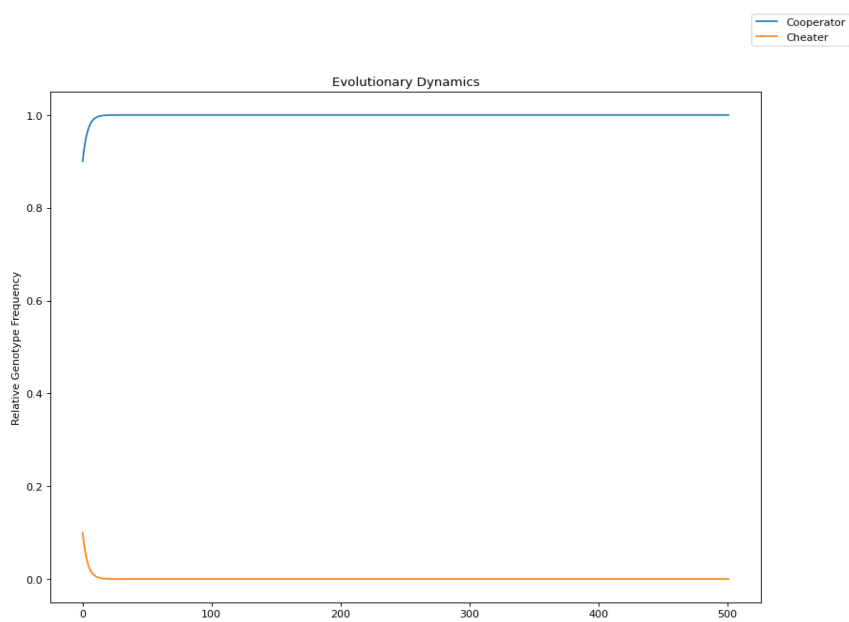
   Paste the code in the box in the Google Colab file and then press Enter/Return.

c. Wait for your code to run. This may take a few seconds.
d. When the code has finished running, you can try changing the sliders to different values to see how the plot changes. Once the sliders are at the desired values, rerun the last cell named "**Plotting the Results.**" You can do this by hovering your cursor over the left side of the cell and clicking the play button.

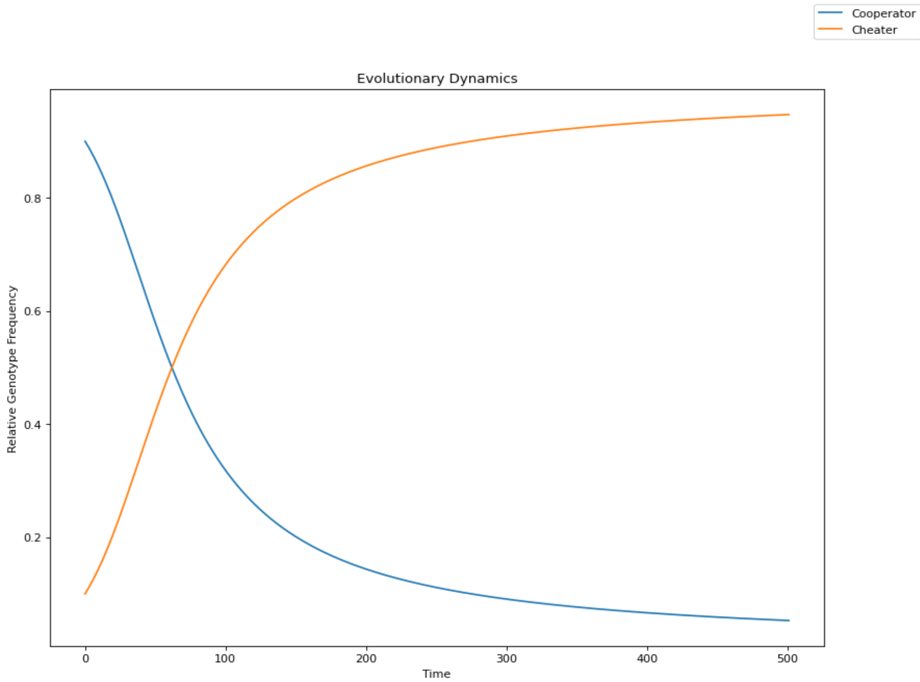


3. Now that we know how to use the simulation, let's consider how changing the conditions (altering the values for ATP coefficient and capture efficiency) would lead to the different kinds of games we have discussed.
    a. What conditions might lead to a **mutually beneficial game**?
    b. What conditions might lead to a **prisoner's dilemma game**?
    c. What conditions might lead to a **snowdrift game**?

4. Let's test your hypotheses! Set the fraction of cooperators to 0.9 for all the following simulations. Run the following simulations:
    a. ATP coefficient = 1, capture efficiency = 0.8
        i. What type of outcome is this? (mutually beneficial, prisoners dilemma, or snowdrift)



b. ATP coefficient = 10, capture efficiency = 0.3
   i. What type of outcome is this? (mutually beneficial, prisoners dilemma, or snowdrift)



c. ATP coefficient = 6, capture efficiency = 0.4
   i. What type of outcome is this? (mutually beneficial, prisoners dilemma, or snowdrift)