Finance of Innovation
[ITMDI 703]

Understand the
"Research and Development" (R&D) Finance

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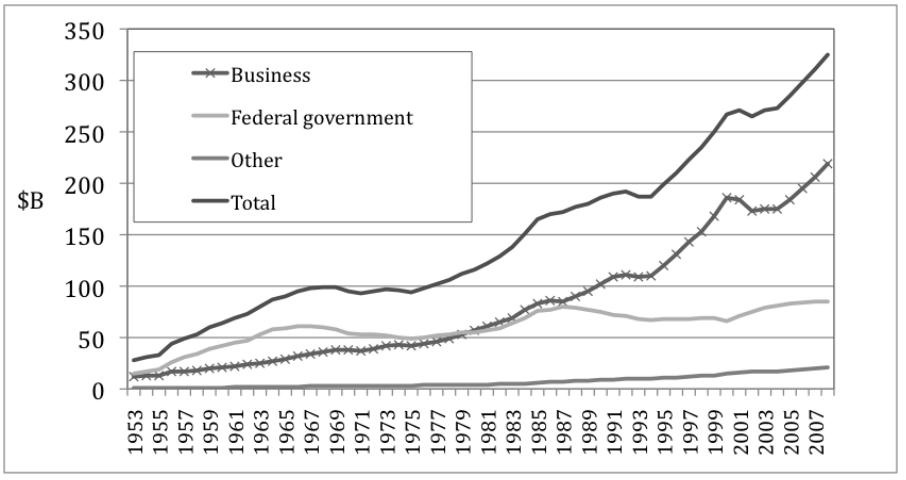
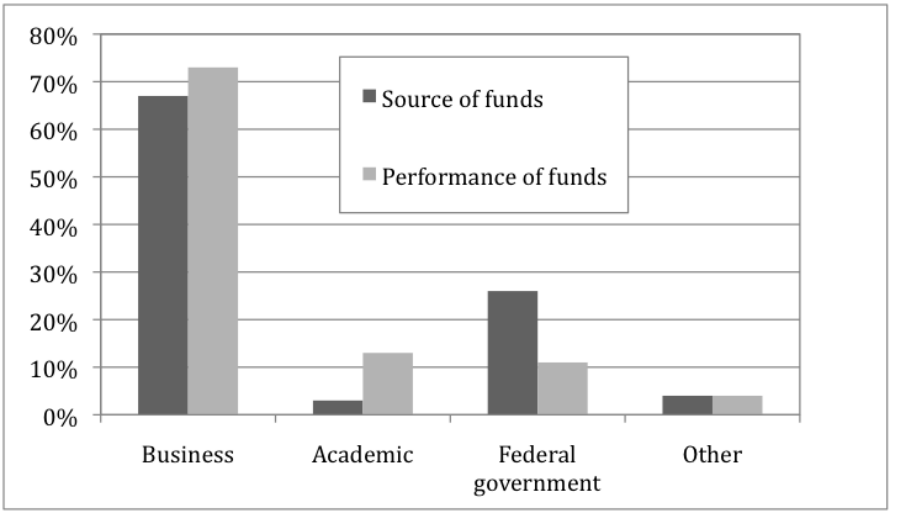
R&D as a % of GDP

Region/country/economy	RD/GDP (%)	Region/country/economy	RD/GDP (%)
North America		Central and Eastern Europe	
United States (2007)	2.68	Russian Federation (2007)	1.12
Canada (2008)	1.82	Turkey (2007)	0.71
Latin America and Caribbean		Czech Republic (2007)	1.54
Mexico (2005)	0.46	Poland (2007)	0.57
Argentina (2007)	0.51	Hungary (2007)	0.97
Western Europe		Romania (2007)	0.53
Germany (2007)	2.54	Slovenia (2007)	1.53
France (2007)	2.08	Slovak Republic (2007)	0.46
United Kingdom (2007)	1.79	East, South, West Asia	
Italy (2006)	1.13	Japan (2007)	3.44
Spain (2007)	1.27	China (2007)	1.49
Sweden (2007)	3.60	South Korea (2007)	3.47
Netherlands (2007)	1.70	Taiwan (2007)	2.63
Austria (2008)	2.66	Singapore (2007)	2.61
Switzerland (2004)	2.90	Pacific	
Belgium (2007)	1.87	Australia (2006)	2.01
Finland (2008)	3.46	New Zealand (2007)	1.20
Denmark (2007)	2.55	Africa and Middle East	
Norway (2007)	1.64	Israel (2007)	4.68
Ireland (2008)	1.45	South Africa (2005)	0.92
Portugal (2007)	1.18	Selected country group	
Greece (2007)	0.58	OECD (2007)	2.29
Luxembourg (2007)	1.63	European Union-27 (2007)	1.77
Iceland (2008)	2.76	G-7 countries (2007)	2.53

U.S. R&D Funding by Source



U.S. R&D by Source and Performer



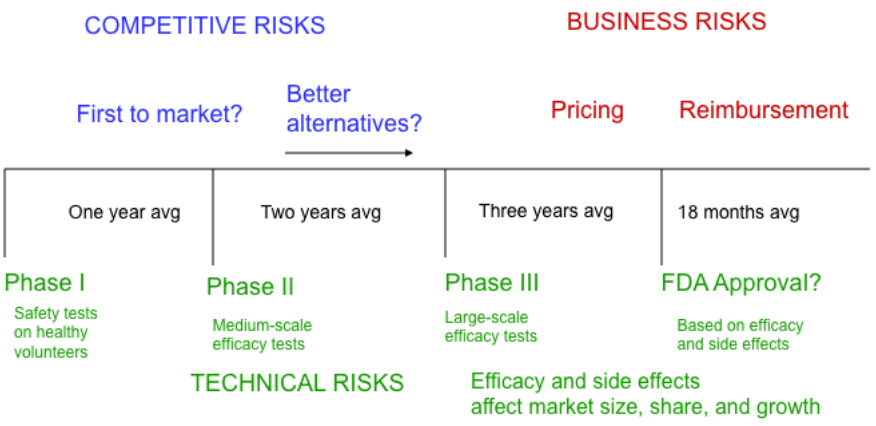
R&D Definitions from the NSF

- *Basic research*: The objective of basic research is to gain more comprehensive knowledge or understanding of the subject under study without specific applications in mind. In industry, basic research is defined as research that advances scientific knowledge but does not have specific immediate commercial objectives, although it may be performed in fields of present or potential commercial interest.
- *Applied research*: The objective of applied research is to gain the knowledge or understanding to meet a specific, recognized need. In industry, applied research includes investigations to discover new scientific knowledge that has specific commercial objectives with respect to products, processes, or services.
- *Development*: Development is the systematic use of the knowledge directed toward the production of useful materials, devices, systems, or methods, including the design and development of prototypes and processes.

R&D Finance

- Themes
  - Nonlinearities: Interactions between risks lead to highly complex models that must be solved using **simulation;**
  - Decisions made over time, leading to **real options;**
  - Multiple decision makers, so that we must use **game theory** to model behavior.
- This themes give rise to three types of risk
  - Technical (=idiosyncratic, use simulation to solve)
  - Business (=systematic, use real options to solve)
  - Competitive (use game theory to solve)

Pharmaceutical R&D



Pharmaceutical R&D: Data

Phase	Mean Time to Next Phase (in months)	Capitalized phase cost (in T $millions)	Probability of reaching phase (in percent)
I	12.3	30.5	100
I	26.0	41.6	71.4
III	33.8	119.2	31.4
Approval	18.0	NA	16.7

Sources: DeMasi et al (2003), Tufts CSDD Outlook 2005, author's calculations

Pharmaceutical R&D: Financing

- How can we finance this cost? Main sources:
  - Largeco: Internal funds
  - Mediumco: Public markets
  - Smallco: Strategic alliances / licensing
  - Newco: VC
- Of course, each size does not exclusively use one type of financing.
- Government and non-profits can partially fund some parts for all types of companies.

Strategic Alliances and Licensing

- Alliance and licensing (a special type of alliance) is the major source of funding (much more than VC) for private and small public biopharma companies.
- Licensing deals can take a wide variety of structures, the most common components are
  - Upfront fees
  - Milestone payments
  - Royalties
  - R&D funding
  - Equity investments

Example of Strategic Alliance

Novartis gets the exclusive worldwide development, manufacturing, and marketing rights to Anadys's ANA975 and other [similar compounds] for chronic hepatitis B and C viruses and other infectious diseases… Novartis will pay a $20M up-front license fee, $550M in regulatory and commercial milestones for the development and marketing of ANA975, including $10M payment upon a successful IND submission (it anticipates a mid-2005 filing). Novartis will provide funding for 80.5 percent of the expenses associated with developing the lead candidate, with Anadys funding 19.5 percent of the costs. Anadys has a co-promotion option to keep 35 percent of the U.S. profits if it pays that percentage of the marketing costs. If Anadys declines the option, it will get royalties on global sales of the resulting product. No equity was exchanged. (Source*: In Vivo*, July/August 2005, p.92)

Trees and Tools

- We use event trees and Monte Carlo simulation to handle problems that do not have sequential decisions (Chapter 20)
- We use game trees and game theory to handle multiple-agent decision problems (Chapter 23).

Some Terminology

- Simulation
  - Monte Carlo simulation
- Discrete random variables
- Continuous random variables
- Event trees
  - Risk nodes
  - Branches
  - Terminal nodes

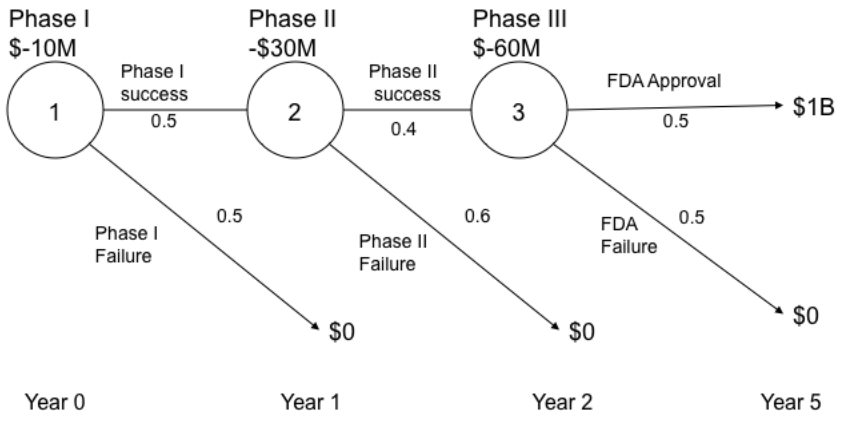
Example 1

Drugco has just begun Phase I trials for Newdrug. Phase I takes one year and costs $10M. Drugco's scientists estimate that the R&D has a 50 percent chance of successfully completing Phase I and moving to Phase II. Phase II takes one year and costs $30M. If Newdrug enters Phase II, the scientists estimate a 40 percent chance of successfully completing Phase II and moving to Phase III. Phase III takes three years (including the time waiting for FDA approval) and costs $60M. If Newdrug enters Phase III, the scientists estimate a 50 percent chance of success (= FDA approval). Drugco management estimates an NPV of $1B at the time of approval. If the drug fails, then it would be worth nothing. The discount rate is equal to the riskfree rate of 5 percent per year. All development costs must be paid at the beginning of the respective phase.

Problems

a) Draw the event tree for the Newdrug project.
b) Find and solve the formula for the NPV of the Newdrug project.
c) Build a Monte Carlo simulation for Newdrug and confirm the same (average) NPV solution as obtained in part (b).

Event Tree



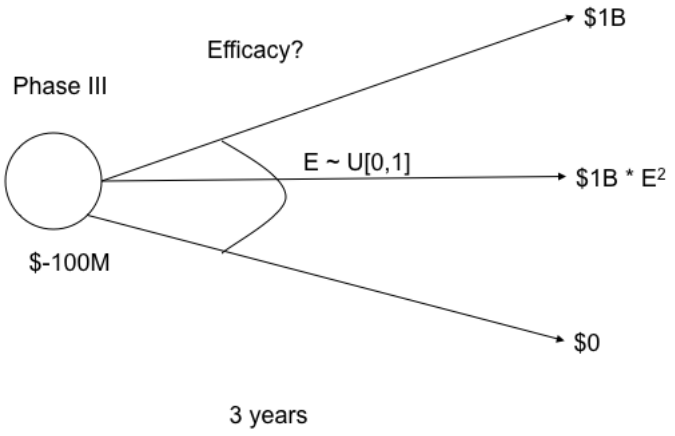
Example 2

Drugco has just begun Phase III trials for Newdrug. For simplicity, we assume that we are sure the drug has no side effects, so all that matters for FDA approval is its efficacy. Efficacy is distributed $E \sim U$ [0,1] and will be learned during three years of Phase III trails. The NPV of the drug after 3 years is \$1B * E^2 (i.e., even with a low efficacy and a high likelihood of FDA failure, we are still allowing for some salvage value for the project). The discount rate is equal to the riskfree rate of 5 percent per year. The total cost of R&D is \$100M and must be paid at the beginning of development.

Problems

a) Draw an event tree for the Newdrug project.
b) What is the NPV of Newdrug if efficacy is set equal to its expected value?
c) Use Monte Carlo simulation to solve for the NPV of the Newdrug project.
d) Why is the answer to part (b) different than the answer to part (c)?

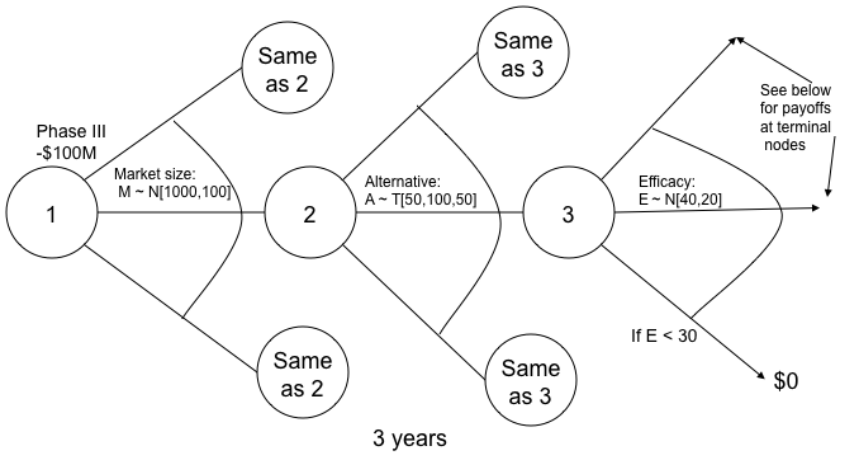
Event Tree



Example 3

- Drugco has just begun Phase III trials for Newdrug at a cost of $100M
  - Phase III trials expected to take two years, and FDA decision one year after that.
  - Efficacy unknown: N(40,20).
  - FDA approval expected if E > 30.
  - Best alternative has efficacy of 50, but could get better over next three years: T(50,100,50).
  - Initial market size unknown: N(1000M,100M).
  - Market growth of 6 percent per year thereafter.
  - Market share: $E^2 / (E^2 + A^2)$
  - Marketing costs of $300M in first year, increasing at 6% per year thereafter.
  - Ten years of patent life remain after approval, NPV of zero after patent expiration.
  - Discount rate of 5 percent per year.

Event Tree



The first year of profits following the terminal nodes with $E \geq 30$ (FDA approval) = $M * E^2 / (E^2 + A^2) - \$300M$.
For years 2 through 10, multiply profits in the previous year by 1.06, then sum with discount of 1.05 per year.

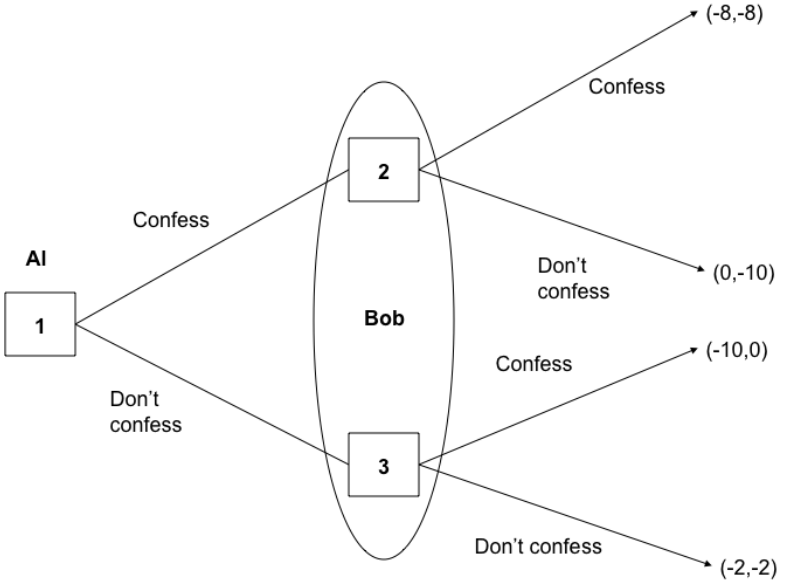
Game Theory

- Game Theory = Multiplayer Decision Problems
- Strategies
- Payoff
- Normal Form
- Extensive Form = Game Tree
- Simultaneous Game
- Sequential Game
- Types of Games
  - Arms Race
  - Zero-sum ("win-lose")
  - Coordination ("win-win")

Example: Prisoner's Dilemma

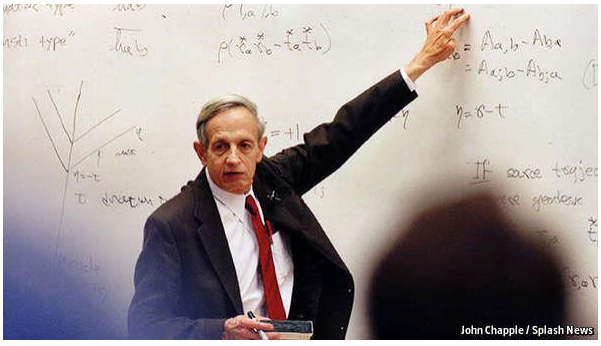
Two people, Al and Bob, have been arrested by the police and are being held in separate rooms. In each room an interrogator explains to the prisoner that he should make things easy for himself and "confess" to the crime. (Whether Al and Bob are actually guilty is immaterial to the problem.) Each prisoner can choose whether or not to confess. If both prisoners confess, then they will both go to jail for eight years. If neither prisoner confesses, then the prosecutors will not be able to convict both defendants of the highest crime, but they will still both go to jail for two years. If, however, only one of the prisoners confesses, then the confessor will be released without any jail time, while the other prisoner will get 10 years.

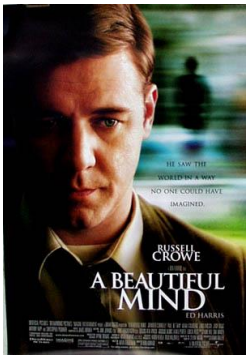
Prisoner's Dilemma, Extensive Form



Nash Equilibrium (NE)

- Each player must play a best response to the strategy of the other player.
  - Thus, in a Nash equilibrium, no player can improve his position by choosing a different strategy.
  - Everyone is playing "a best response to a best response"

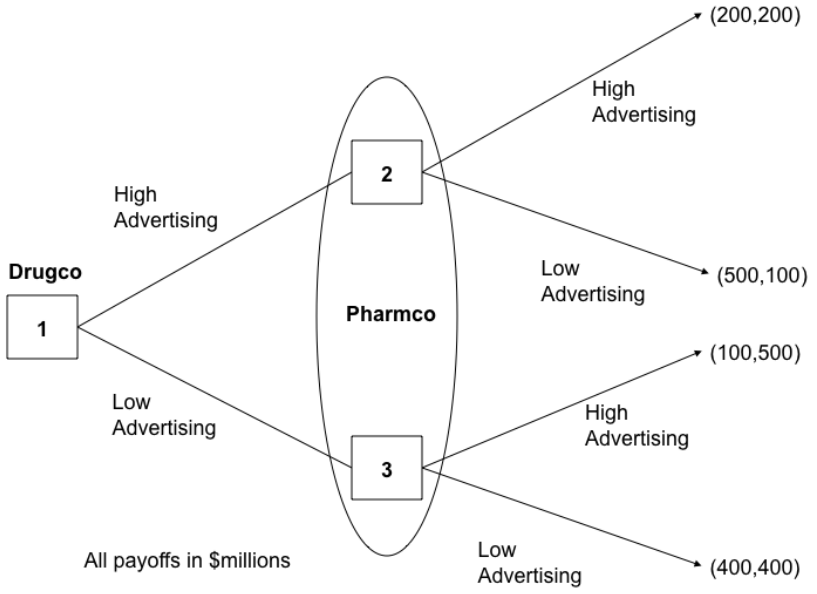




Example: Advertising Arms Race

Drugco and Pharmco produce the two leading drugs to treat severe flu symptoms. These are strong medications available only by prescription, and both firms market their medicines heavily to physicians. Both firms are considering large direct-to-consumer advertising plans. Advertising is very costly, but it would increase awareness of the drugs and help each firm in its competitive position. Each firm can independently choose to be aggressive in the direct-to-consumer market by choosing *high advertising* or to be less aggressive by choosing *low advertising*. If only one of the two firms chooses *high advertising*, then the NPV of that firm's product (including advertising costs) would be $500M, whereas the NPV of the *low advertising* firm would be $100M. If both firms choose *high advertising*, then the NPV of each product would be $200M. If both firms choose *low advertising*, then the NPV of each product would be $400M.

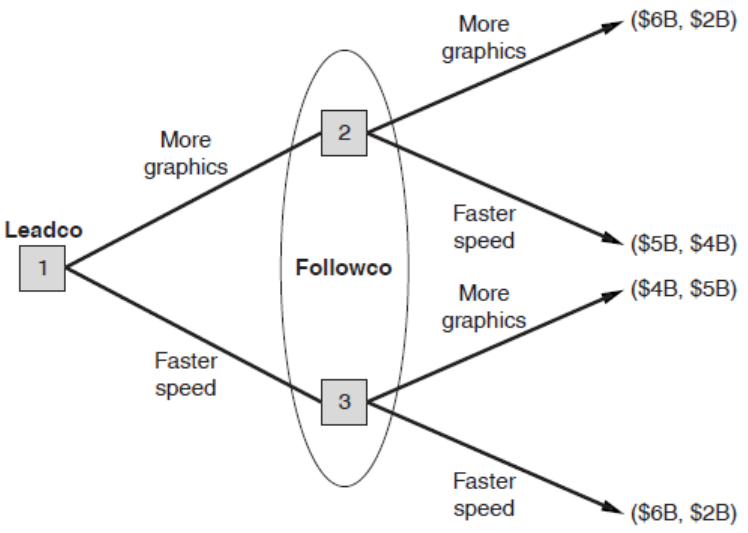
Advertising Game, Extensive Form



Example: Leader-Follower Game

Leadco is the market-leading producer of microprocessors for home and small business computers. Followco is Leadco's closest competitor in this market. Both firms are currently working on their next-generation microprocessor. These development projects, carried out in great secrecy, face typical constraints for microprocessor development: customers demand many new features, but adding features tends to reduce processor speed. Both Leadco and Followco believe that the majority of customers want to have more graphics capabilities on the chip, but the reduction in speed will turn off other customers. Both companies must decide how much more graphics capability to add, knowing that this addition will reduce the processor speed. We summarize the contrasting goals with two possible strategies for each firm: more graphics and faster speed. With a larger installed-base and more brand awareness, Leadco would like to have the same strategy as Followco because this symmetry will tend to preserve their current lead. If both companies choose the same strategy, then Leadco would maintain a 75 percent share of the market, and their processor would have an NPV of $6B, with $2B for Followco. On the other hand, Followco would like to adopt the opposite strategy from Leadco because they would then have the opportunity to steal some of Leadco's installed base. If the two firms choose different strategies, then the firm with more graphics will have an NPV of $5B, and the firm with faster speed will have an NPV of $4B.

Leader-Follower Game, Extensive Form



Minimax solution

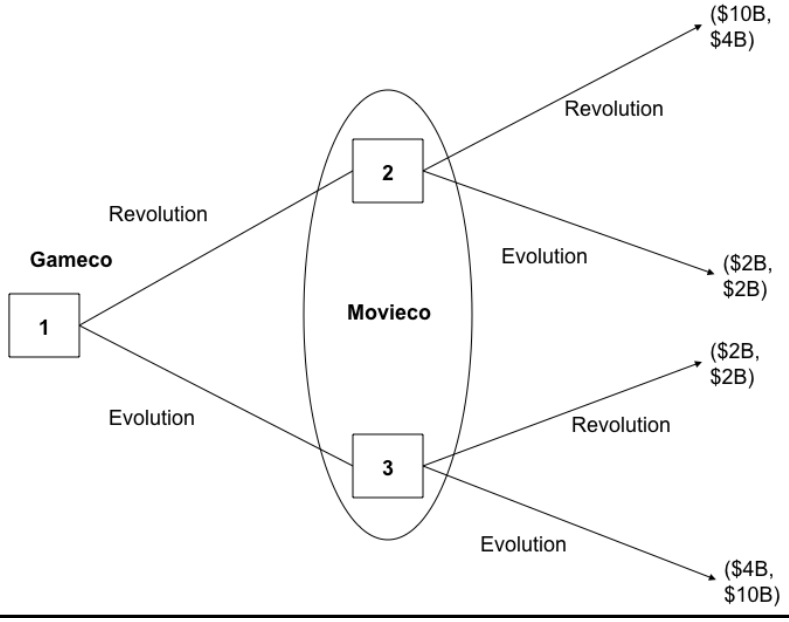
- Minimizing the possible loss for a worst case (maximum loss) scenario.
- Originally formulated for two-player zero-sum game theory, covering both the cases where players take alternate moves and those where they make simultaneous moves.

Example: Standards Game

Gameco and Movieco are the leading developers of DVD technology. In the past, these two companies were able to agree on identical technical standards, but they are now embroiled in a fierce debate about the next generation of technology. Gameco believes that the time is ripe for a revolutionary change in DVD technology that would provide much larger storage capacity and allow for highly complex interactive games. Movieco, on the other hand, favors a more evolutionary change that would maintain a higher degree of backward compatibility.

Because the companies are unable to agree on a standard technology, they have continued with separate development projects. Other content providers are reluctant to choose sides, fearing that they may pick the wrong company to back. This delay is damaging the long-term sales potential of both technologies. If the two companies are unable to settle on a single technology, then each project would be worth $2B. Both companies would do better if they could agree on a single standard—but which one? The revolutionary standard would favor Gameco, with an expected NPV of $10B versus only $4B for Movieco. The evolutionary standard would favor Movieco, with an expected NPV of $10B versus only $4B for Gameco. Although this is an ongoing battle with no clear endpoint, we choose to model it as a single-stage simultaneous game, where each company must decide on a standard.

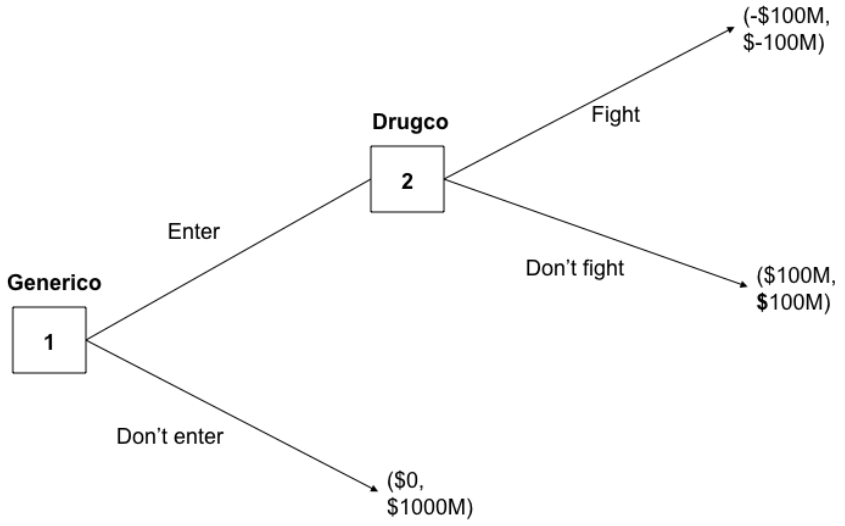
Standards Game, Extensive Form



Example: Entry Game

Drugco sells *Leaufleau*, the market-leading drug for hypertension. This drug is about to lose patent protection for its key ingredient. Generico, a maker of generic drugs, is considering entry into the hypertension market with the chemical equivalent of *Leaufleau*. Under law, if Generico is the first company to gain approval for a generic version of *Leaufleau*, then they will be allowed six months as the only generic competitor. After this six months is over, other companies can enter the market with their own versions. As soon as generic competition intensifies, the profits for both the incumbent (Drugco) and the first generic (Generico) would fall significantly. Drugco would like to postpone this date for as long as possible by "scaring" Generico out of the market. As Generico plans to introduce their drug, Drugco files expensive lawsuits claiming infringement of patents related to the manufacturing of *Leaufleau* and prepares to drop the price of *Leaufleau* to keep consumers from switching to the generic form during Generico's six-month exclusivity period. If Drugco succeeds in scaring Generico away from entry, then Drugco will increase their NPV by $1B, and Generico will have an NPV of 0. If Generico enters the market and Drugco chooses to fight with these measures, then both companies will lose $100M. If Generico enters and Drugco decides not to fight, then both companies will make $100M.

Entry Game, Extensive Form

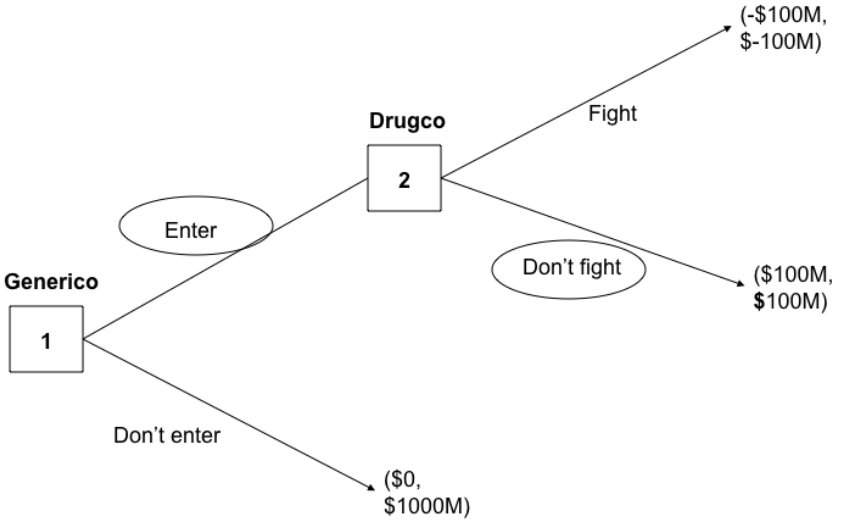


Subgame-Perfect Nash Equilibrium (SPNE)

Step 1) Identify all "subgames" in the extensive form.

Step 2) Solve backwards, using NE in each subgame.

Entry Game, Extensive Form, with Subgame Perfect Strategies Circled



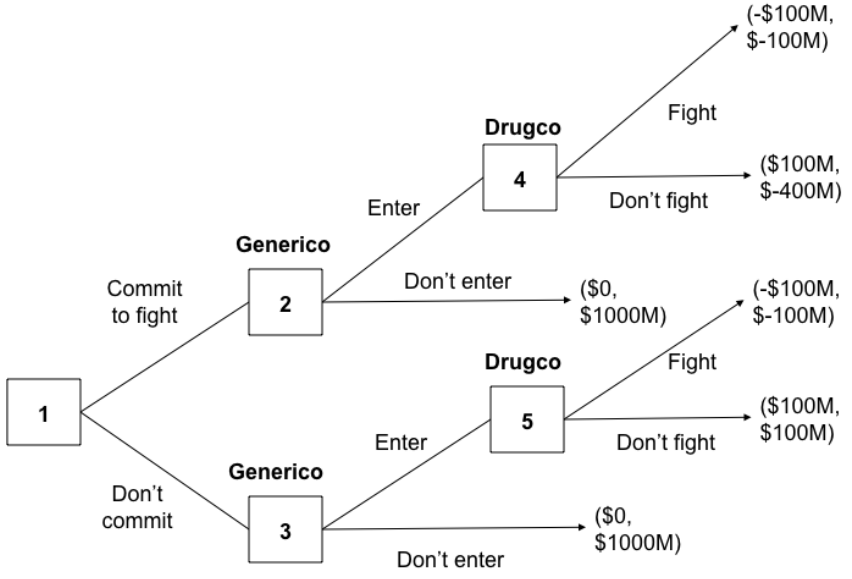
Example: Entry Game (Continue)

Now, we add an additional move to the game. Before Generico decides whether to enter, Drugco can commit to a fight. Drugco makes this commitment by placing $500M in an escrow account with a specialized "commitment agent". The terms of this escrow state that if Drugco fails to fight, then the $500M will be forfeited to the commitment agent. In all other respects, the

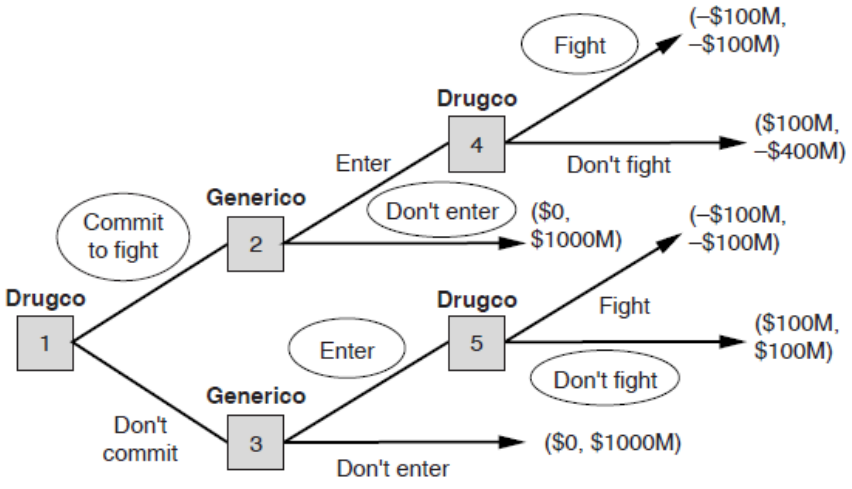
payoffs are the same as before.

Draw the extensive form for this game, identify the subgames, circle the best responses in each subgame, and solve for the SPNE.

Entry Game, with Commitment Extensive Form (1)



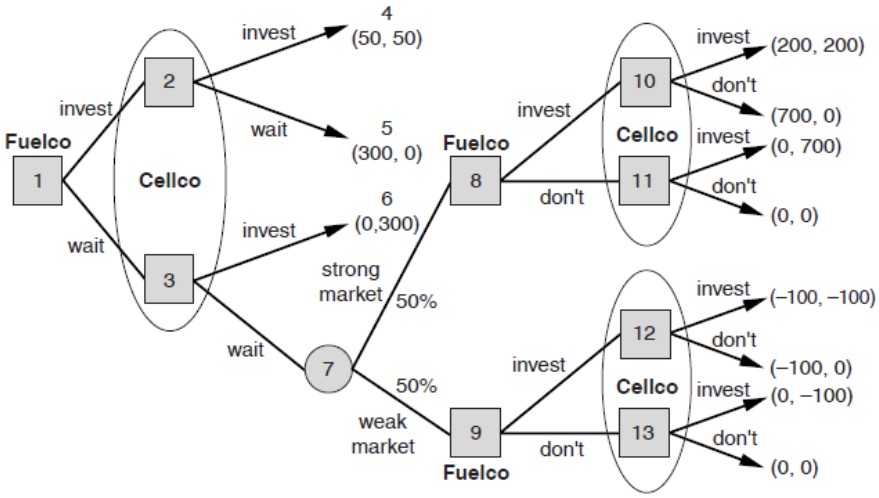
Entry Game, with Commitment Extensive Form (2)



Exercise: FUELCO'S Project with competition

Fuelco is considering a consumer application for their patented fuel-cell technology. They have already completed several R&D projects with this technology, so they have eliminated the technical risk for this new project. To begin producing and marketing to the consumer market would require a new investment of $200M, to be paid in one year. The value of Project C depends on consumer demand and also depends on whether a competitor, Cellco, also enters this market. To keep things (relatively) simple, we assume that the beta for the project is zero and that the risk-free rate is also zero, so all discount rates are zero for the both firms. At time 0, Cellco and Fuelco each decide whether to invest or wait. If one firm invests and the other waits, then the investing firm will get the whole market and have an NPV of $300M, whereas the waiting firm will have an NPV of $0. If both firms invest, then competition will drive down the profits of both firms, which will each have an NPV of $50M. (All NPVs described in this problem are net of the $200M investment, when the investment is made. Thus, the gross NPV if both firms invest would be $250M.) If both firms wait, then they both get to observe whether demand is "high" or "low", after which each firm decides whether or not to invest. If demand is "high" (50 percent chance) and only one firm chooses to invest, then that firm receives an NPV of $700M, and the other firm receives an NPV of $0. If neither firm invests, then both firms receive an NPV of $0. If both firms invest, then each firm receives an NPV of $200M. If demand is "low" (50 percent chance), and only one firm chooses to invest, then that firm receives a negative NPV of 2$100M, and the other firm receives an NPV of $0. If neither firm invests, then both firms receive an NPV of $0. If both firms invest, then each firm receives a negative NPV of 2$100M.

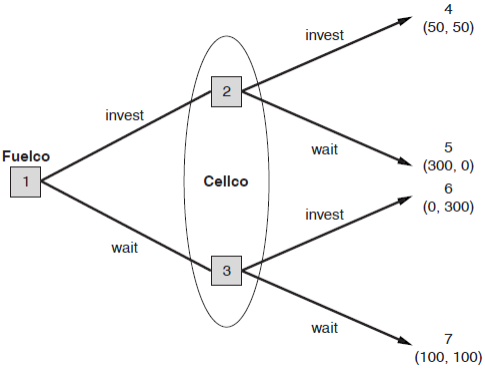
FUELCO'S Project with competition, Extensive Form



FUELCO'S Project with competition, Normal Form

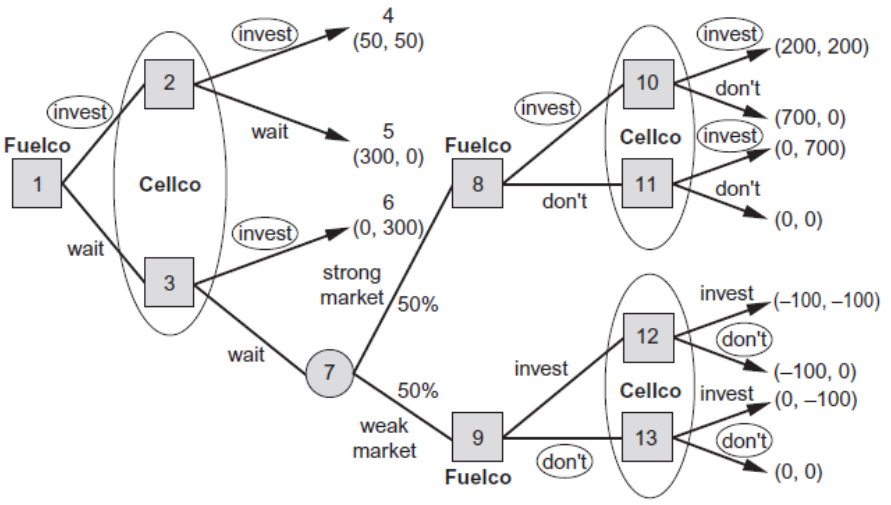
Fuelco \ Cellco	Invest	Don't Invest
Invest	$200M, $200M	$700 M, $0M
Don't Invest	$0M, $700M	$0M, $0M

Fuelco \ Cellco	Invest	Don't Invest
Invest	–$100M, –$100M	–$100M, $0M
Don't Invest	$0M, –$100M	$0M, $0M



Fuelco \ Cellco	Invest	Wait
Invest	$50M, $50M	$300M, $0M
Wait	$0M, $300M	$100M, $100M

FUELCO'S Project with competition, Best responses circled



Summary

In this course, we have performed two kinds of analysis:

- Positive analysis: aims to describe actual behavior (examples: studies of VC returns (chapters 3 and 4), the performance of specific VC investments (Chapter 7), and the frequencies of various contractual terms (chapters 2 and 8)
- Normative analysis aims to describe optimal behavior (examples: the modified VC method (Chapter 9), Game theory)