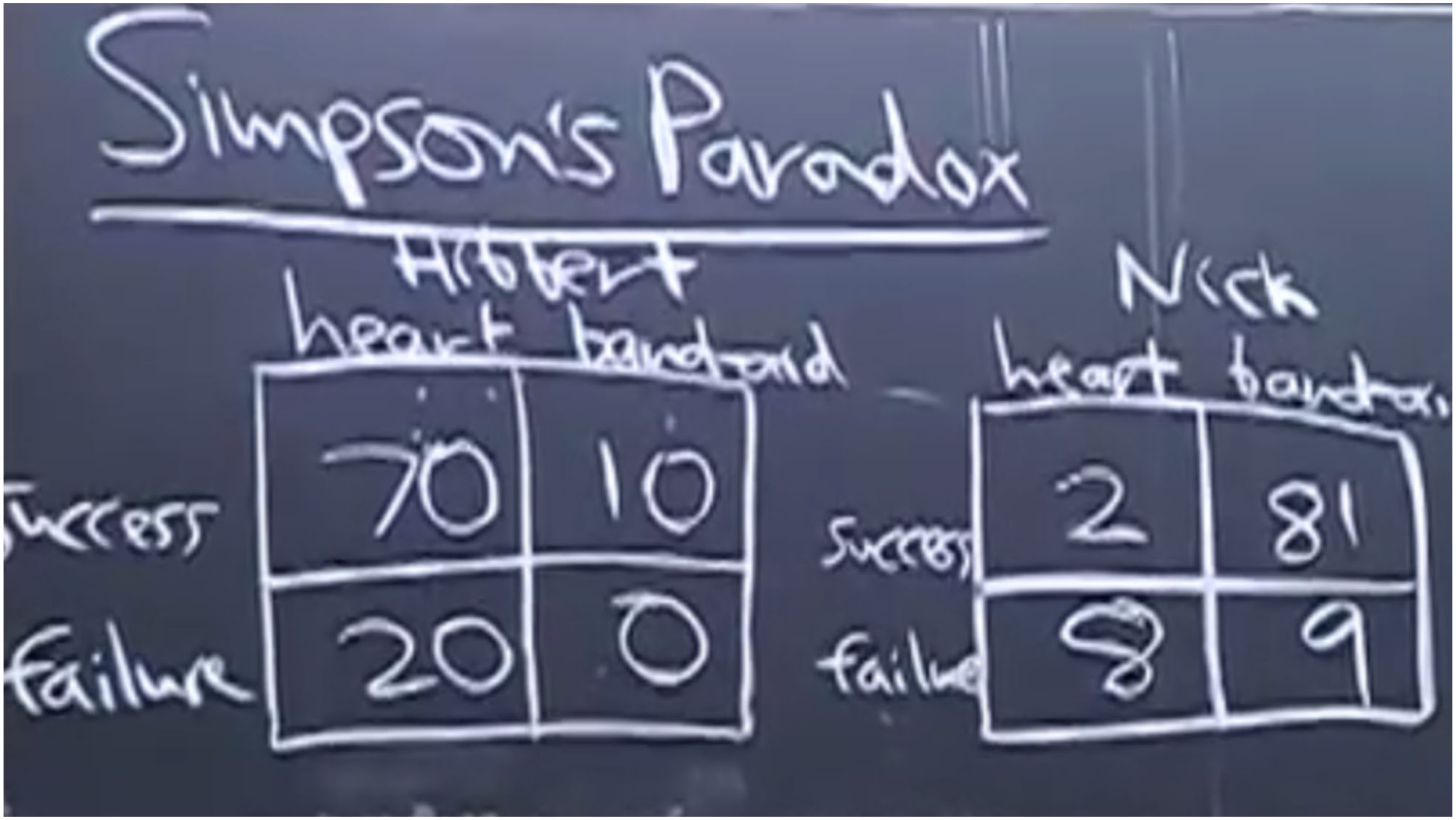
Simpson’s paradox

Edward Hugh Simpson
(10 December 1922 – 5 February 2019)
was a British codebreaker, statistician
and civil servant.
"The Interpretation of Interaction
in Contingency Tables“, Journal of the Royal Statistical Society, 1951

Is it possible for one doctor to have a **higher** success rate than another doctor in **every** type of treatment he performs but to have a **lower** **overall** success rate across all treatment types?

Dr. Hibbert

Dr. Nick

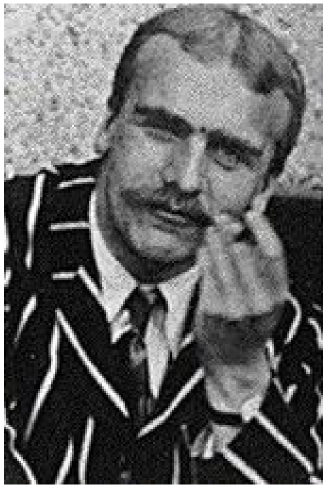


Dr. Hibbert: success rate =80%

Dr. Nick: success rate =83%

Simpson's paradox might explain altruism

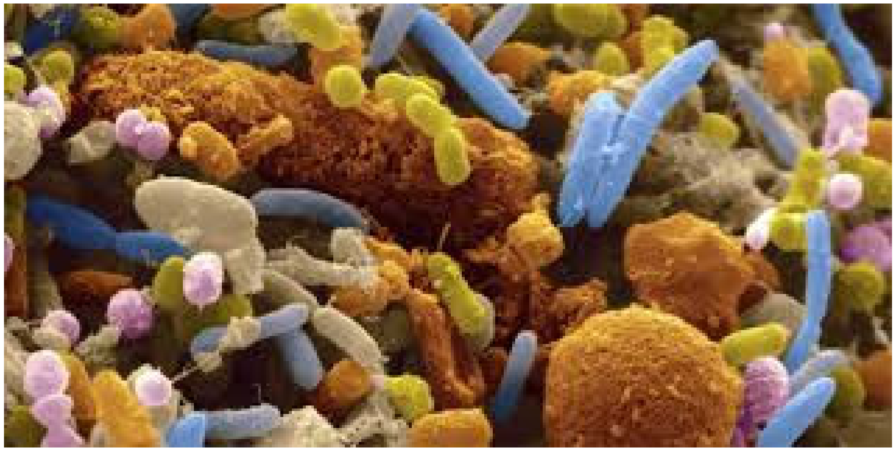
- Darwinian evolution has a problem with altruism
- "Selfish genes" do not care about others
- J. B. S. Haldane, (1892-1964) British geneticist, evolutionary biologist



- When asked if he would give his life to save a drowning brother answered: "No, but I would to save two brothers or eight cousins"
- Altruism in some insect colonies like ants is because they are all genetically similar.

Altruism in bacteria

- Bacteria live in communities in close proximity to each other
- Individual bugs spend significant resources to produce extracellular molecules, excrete them outside of the cell to share with others. **That slows their growth**
  - Examples: extracellular enzymes, biofilm components, antimicrobial and anti-immune agents
- Cheaters have faster growth rate
  - They can take over by not producing any shared molecules
- **<u>Evolutionary paradox: how bacteria can be altruistic?</u>**



Chuang, Rivoire, and Leibler's answer

Simpson's Paradox in a Synthetic Microbial System

John S. Chuang,* Olivier Rivoire, Stanislas Leibler

The maintenance of "public" or "common good" producers is a major question in the evolution of cooperation. Because nonproducers benefit from the shared resource without bearing its cost of production, they may proliferate faster than producers. We established a synthetic microbial system consisting of two *Escherichia coli* strains of common-good producers and nonproducers. Depending on the population structure, which was varied by forming groups with different initial compositions, an apparently paradoxical situation could be attained in which nonproducers grew faster within each group, yet producers increased overall. We show that a simple way to generate the variance required for this effect is through stochastic fluctuations via population bottlenecks. The synthetic approach described here thus provides a way to study generic mechanisms of natural selection.

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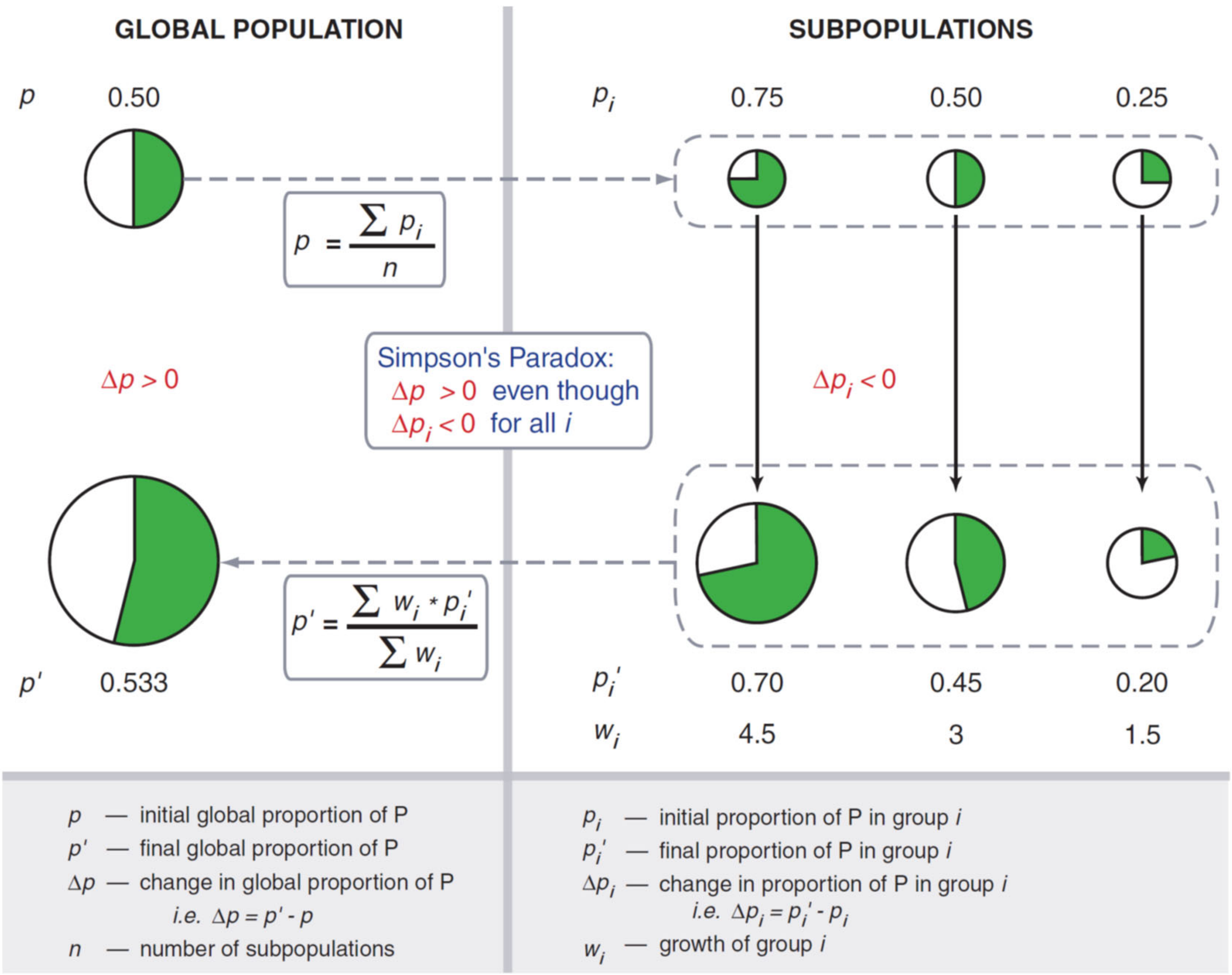
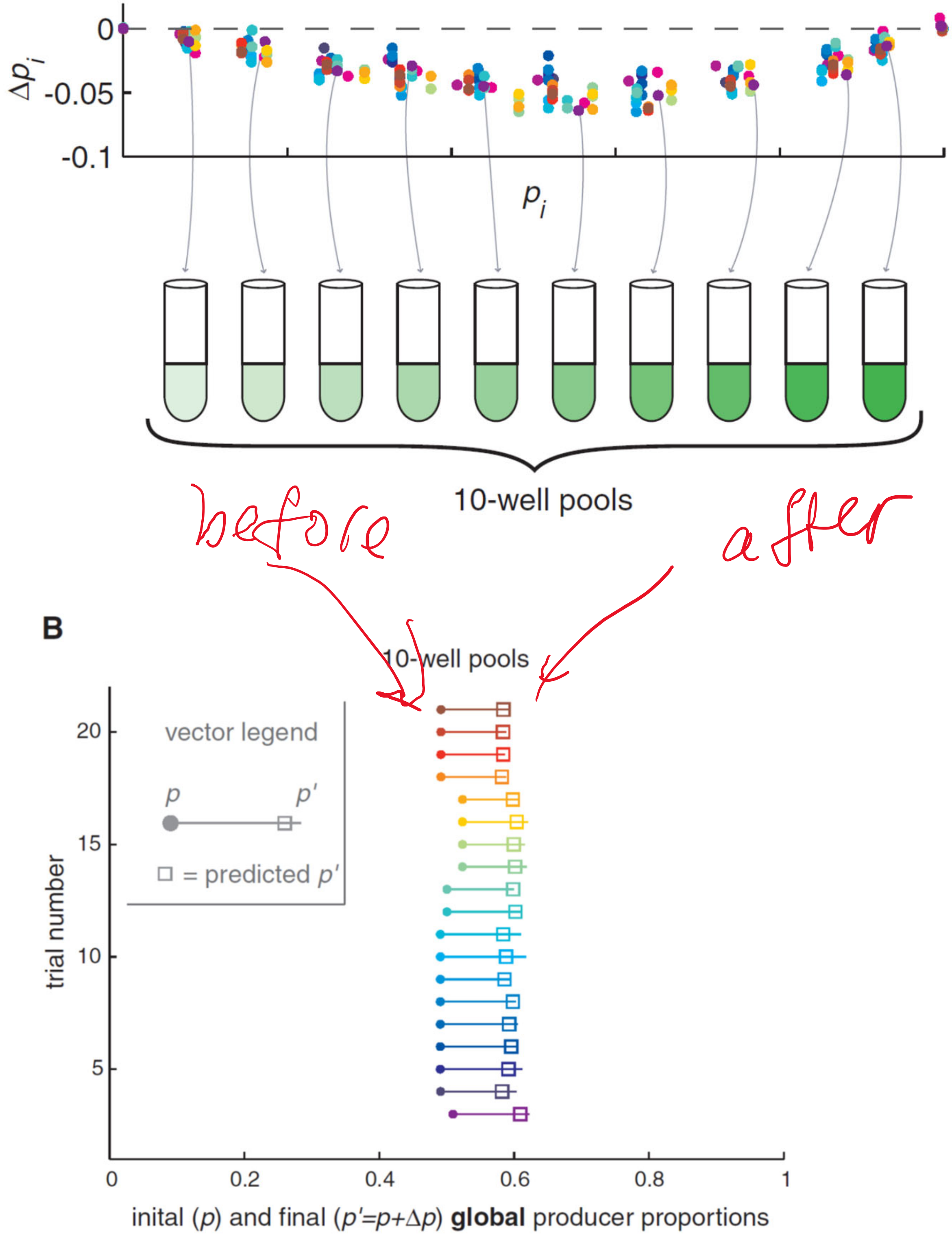
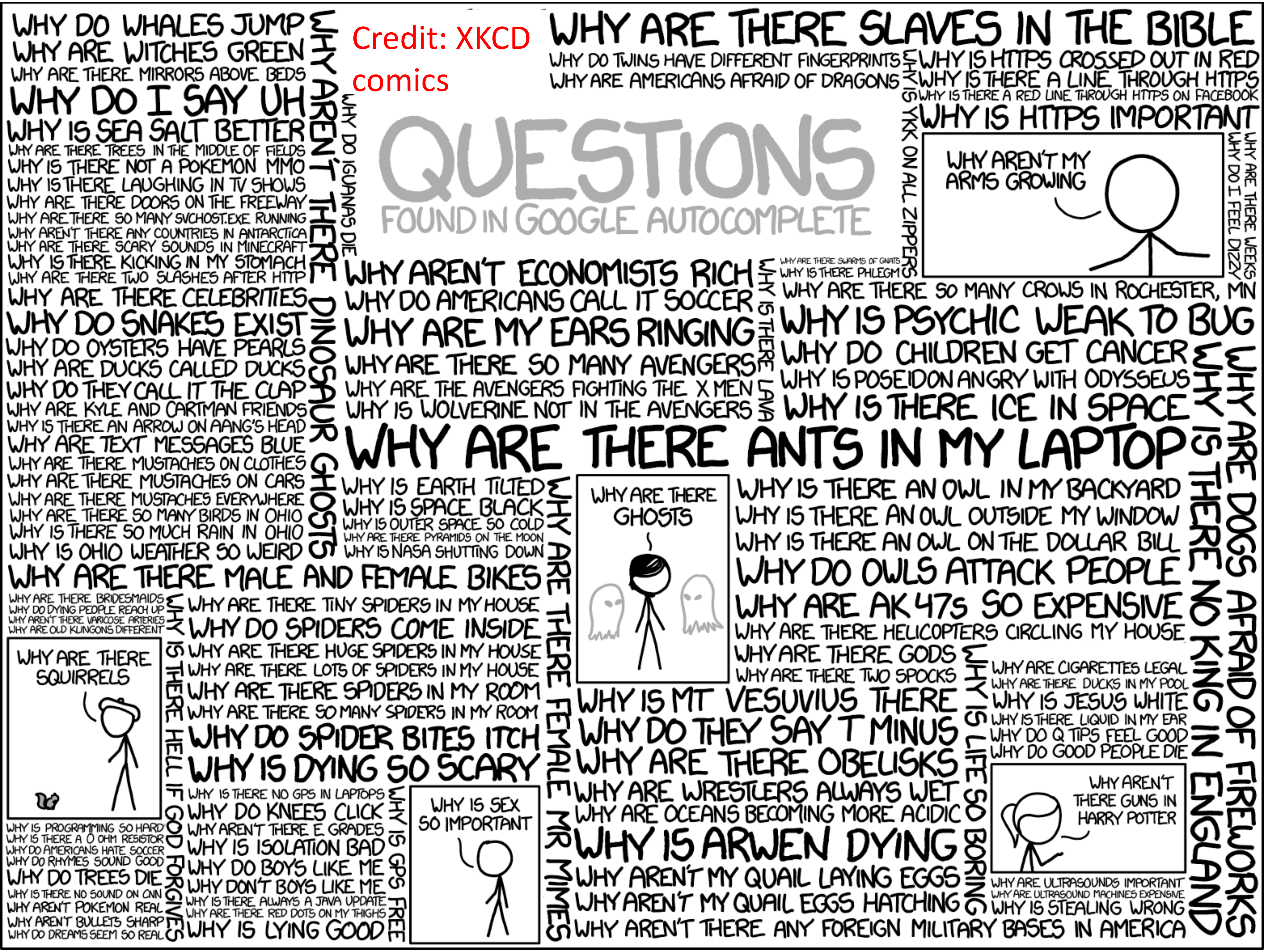
- The common good was a membrane-permeable Rhl autoinducer molecule rewired to activate antibiotic (chloramphenicol; Cm) resistance gene expression.



Fraction of altruists in
each of individual
test tubes dropped

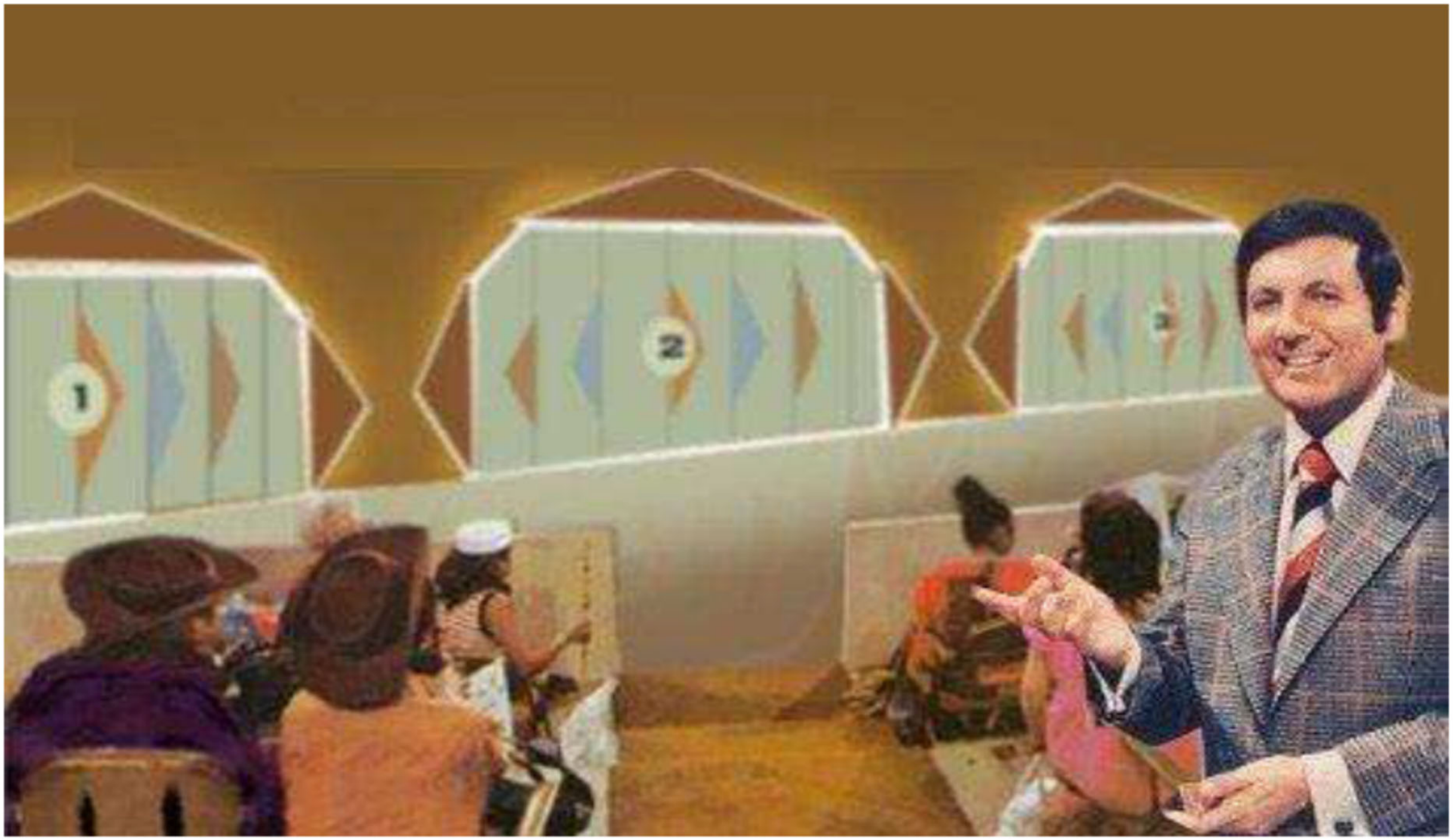


Yet the overall fraction of
altruists in
all test tubes combined
increased



Credit: XKCD comics

Monty Hall problem



Monty Hall OC, OM (born Monte Halparin)

August 25, 1921 – September 30, 2017

was a Canadian-American game show host, producer, and philanthropist

Game show “Let’s Make a Deal” aired 1963-now

Monty Hall problem

- In *Make a Deal* there are three closed doors. Behind a random one of these doors is a car; behind the other two are goats. The contestant does not know where the car is, but Monty Hall does.
- After the contestant picks a door Monty always opens one of the remaining doors, one he knows does not hide the car. If the contestant has already chosen the door with the car behind, Monty is equally likely to open either of the two remaining doors.
- After Monty has shown a goat behind the door that he opens, the contestant is always given the option to switch doors.
- What is the probability of winning the car under the switching and non-switching strategies?

Monty Hall problem. What strategy gives you a better chance to win the car?

A. Better to switch doors
B. Better not to switch doors
C. Switching does not matter
D. The answer depends on the phase of the moon
E. I don't know

Get your i-clickers

Monty Hall problem. What strategy gives you a better chance to win the car?

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E. I don't know

Get your i-clickers

Don’t feel bad if you guessed wrong

- When first presented with the Monty Hall problem an overwhelming majority of people assume that each door has an equal probability and conclude that switching does not matter
- Out of 228 subjects in one study, only 13% chose to switch
- Paul Erdős, one of the most prolific mathematicians in history, remained unconvinced until he was shown a computer simulation confirming the predicted result
- Pigeons repeatedly exposed to the problem show that they rapidly learn always to switch, unlike humans

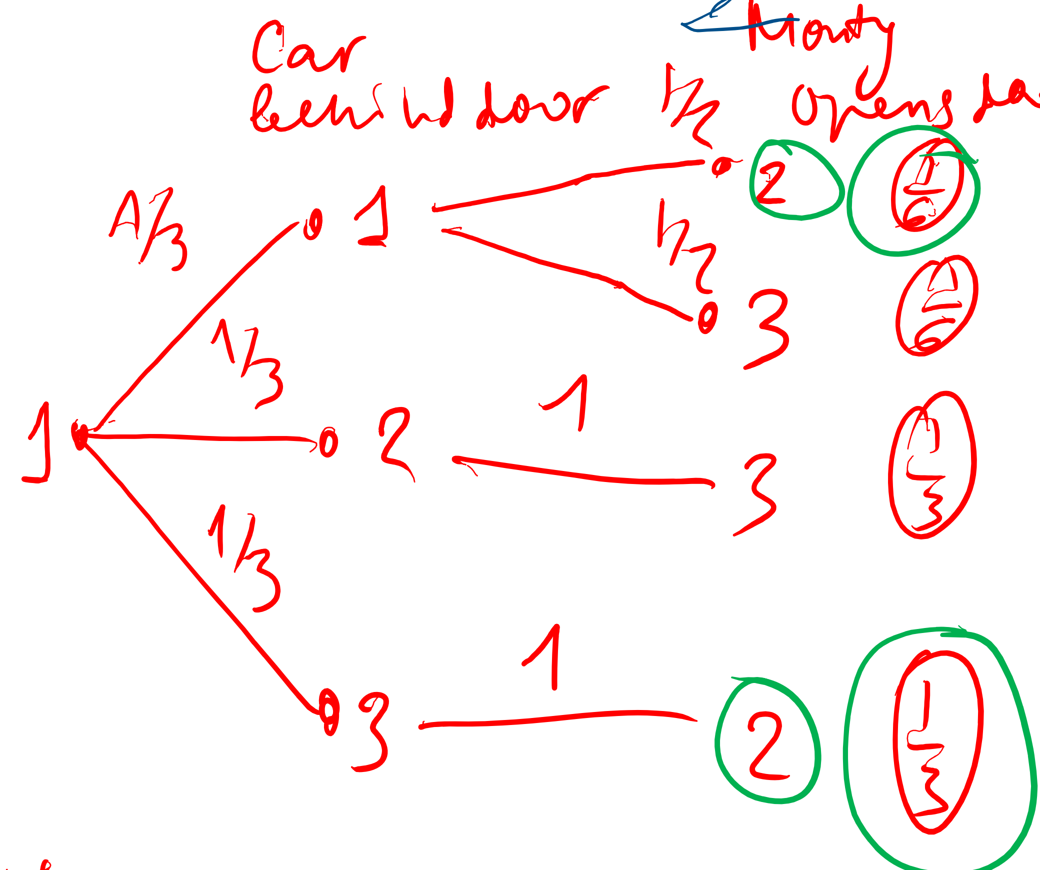
Solution #1 (intuitive)

- With Prob=1/3 you guess the car door right: you loose the car if you switch
- With Prob=2/3 you got it wrong and picked a goat door. Then Monty opens another goat door. What is left is the car door. You win the car if you switch!

Solution #2.
Tree & conditional probabilities

Solution #2.
Tree & conditional probabilities

Contestant chooses door 1



conditional probability

$$P(\text{Monty opens door 2} \mid \text{car behind door 1}) = \frac{1}{2}$$

If Monty opened door 2

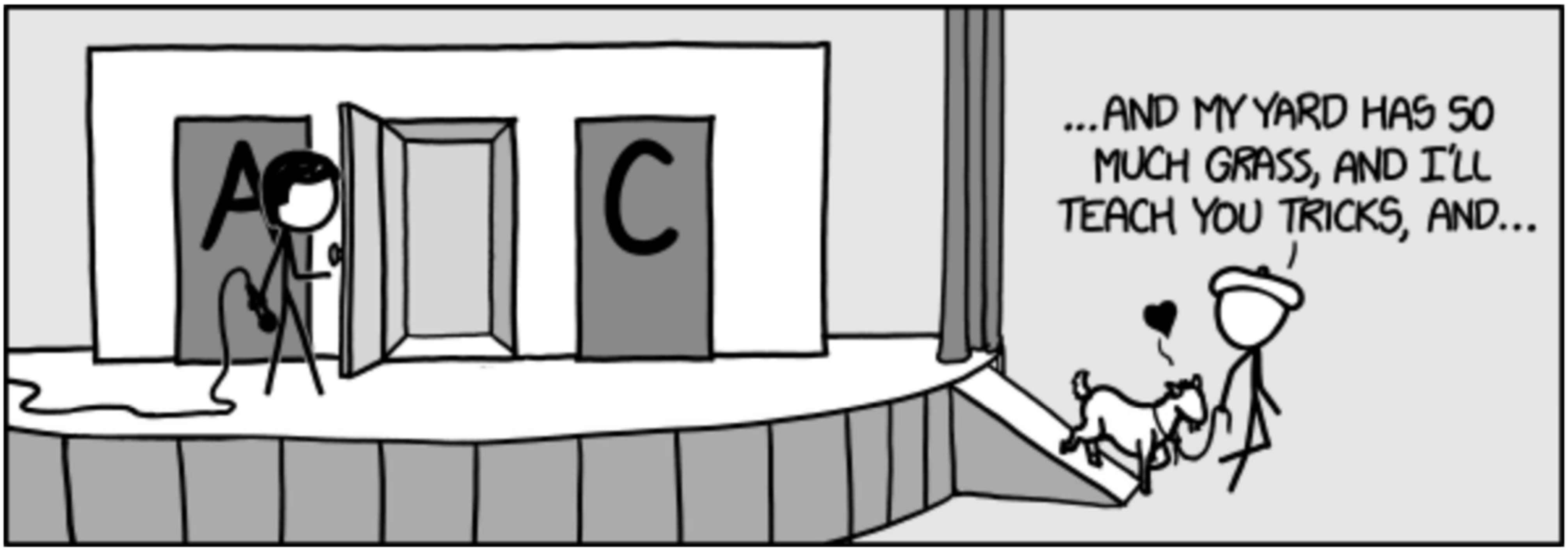
$$\text{Prob}(\text{win by switching}) = \frac{\frac{1}{3}}{\frac{1}{3}+\frac{1}{6}} = \frac{2}{3}$$

$$\text{Prob}(\text{win by staying}) = \frac{1/6}{1/3+1/6} = \frac{1}{3}$$

A more detailed tree diagram

- Shinyapp website
  https://dacalderon.shinyapps.io/montyhall/

  Thanks to my former BIOE 505 student,
  Alejandra Zeballos Castro, for bringing it to my attention



comic credits: xkcd

Let's check the theory by playing the dame

Go to
https://dacalderon.shinyapps.io/montyhall/

- Tables 1,3,5 will play "switch the door" strategy
- Tables 2,4,6 will play "same door" strategy
- Play at least 30 rounds (more is better)
- In the end we will **add up the numbers from all tables**

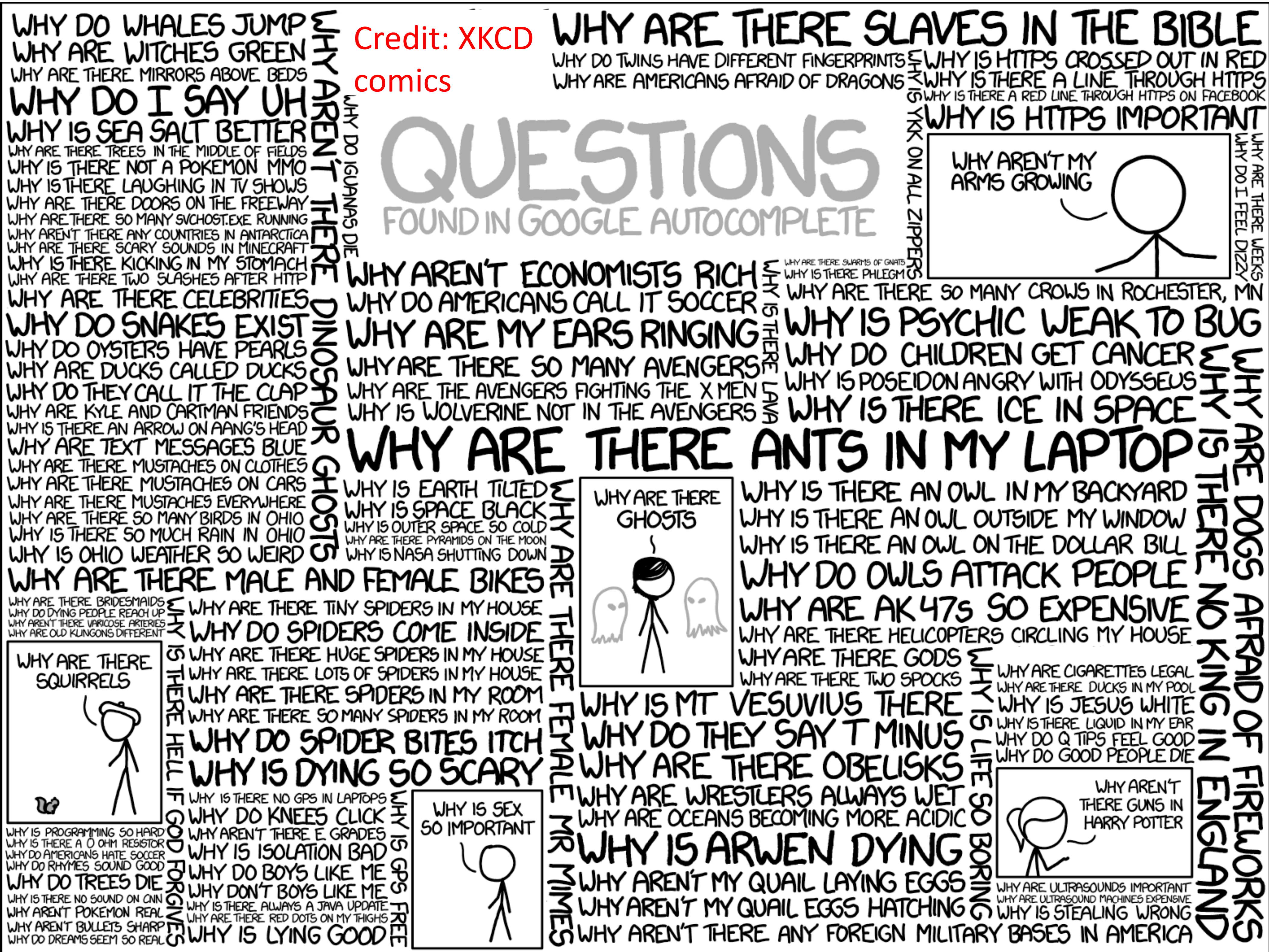
	Switch strategy			No switch strategy	
Table	Played	Won	Table	Played	Won
1	30	18	2	30	8
3	30	15	4	30	10
5			6		
	60	33		60	18
P(win)	0.55			0.3	

Let’s check with more random experiments

- **Stats=??;**
- **%set Stats large...**
- **switch_count=0; noswitch_count=0; %set 0 at the beginning**
- **for n = 1:Stats**
- **a = randperm(3); %Monty places two goats and the car at random**
- **%a(1) -goat, a(2) -goat, a(3) - car**
- **i= floor(3.*rand)+1; %you select the door!**
- **% SWITCH STRATEGY**
- **if(i == a(1)) switch_count=switch_count+??; %a(2)-opened, switch to a(3), car!**
- **elseif (i == a(2)) switch_count = switch_count + ??;%a(1) opened, switch to a(3), car!**
- **else switch_count = switch_count + ??; %a(1)/a(2) opened, switch to a(2)/a(1), no car :-(**
- **end**
- **% NO SWITCH STRATEGY**
- **if(i == a(1)) noswitch_count = noswitch_count + ??; %a(2)-opened, no car :-(**
- **elseif (i==a(2)) noswitch_count = noswitch_count + ?? %a(1)-opened, no car :-(**
- **else noswitch_count = noswitch_count + ??; %a(1) or a(2)-opened, car!**
- **endend;**
- **disp('probability to win a car if switched doors=');**
- **disp(num2str(switch_count./??)); %# of cars with switching**
- **disp('probability to win a car if did not switch doors=');**
- **disp(num2str(noswitch_count./??)); %# of cars w/o switching**

Matlab program

- B=10000; %set B large...
- cars=0; carn=0; %set 0 at the beginning
- for i = 1:B
- a = randperm(3); %Monty places two goats and the car at random
- %a(1) -goat, a(2) -goat, a(3) - car
- i= floor(3.*rand)+1; %you select the door!
- % SWITCH STRATEGY
- if(i == a(1)) cars=cars+1; %a(2)-opened, switch to a(3), car!
- elseif (i == a(2)) cars = cars + 1 ;%a(1) opened, switch to a(3), car!
- else cars = cars + 0; %a(1)/a(2) opened, switch to a(2)/a(1), no car!
- end
- % SWITCH STRATEGY
- if(i == a(1)) carn = carn + 0; %a(2)-opened, no car
- elseif (i==a(2)) carn = carn + 0; %a(1)-opened, no car
- else carn = carn + 1; %a(1) or a(2)-opened, car!
- end
- end;
- disp('probability to win a car if switched doors=');
- disp(num2str(cars./B)); %# of cars with switching
- disp('probability to win a car if did not switch doors=');
- disp(num2str(carn./B)); %# of cars w/o switching



Credit: XKCD comics

Discrete Probability Distributions

Random Variables

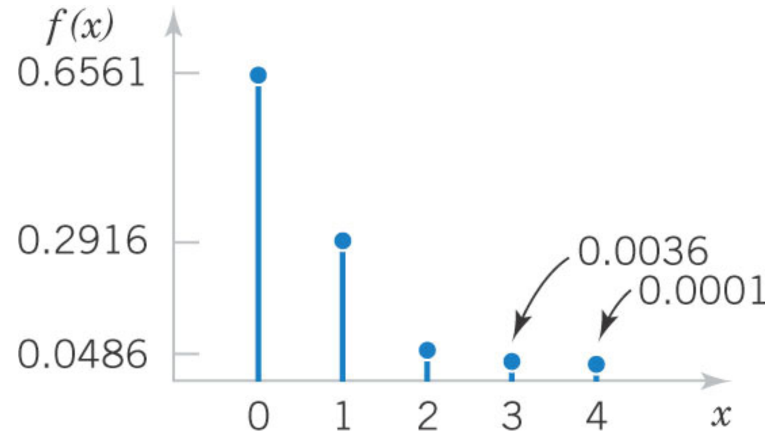
- A variable that associates a number with the outcome of a random experiment is called a random variable.
- Notation: random variable is denoted by an uppercase letter, such as X. After the experiment is conducted, the measured value is denoted by a lowercase letter, such a x. Both X and x are shown in italics, e.g., $P(X=x)$.

Continuous & Discrete Random Variables

- A discrete random variable is usually integer number
  - N - the number of p53 proteins in a cell
  - D - the number of nucleotides different between two sequences
- A continuous random variable is a real number
  - C=N/V – the concentration of p53 protein in a cell of volume V
  - Percentage (D/L)*100% of different nucleotides in protein sequences of different lengths L (depending on the set of L's may be discrete but dense)

Probability Mass Function (PMF)

- I want to compare all 4-mers in a pair of human genomes
- X – random variable: the number of nucleotide differences in a given 4-mer
- Probability Mass Function: f(x) or P(X=x) – the probability that the # of SNPs is exactly equal to x



Probability Mass Function for the # of mismatches in 4-mers

$P(X=0)$ =	0.6561
$P(X=1)$ =	0.2916
$P(X=2)$ =	0.0486
$P(X=3)$ =	0.0036
$P(X=4)$ =	0.0001
$\sum_x P(X=x)$=	1.0000

Cumulative Distribution Function (CDF)

	x	$P(X=x)$	$P(X\le x)$	$P(X>x)$
	-1	0.0000	0.0000	1.0000
	0	0.6561	0.6561	0.3439
	1	0.2916	0.9477	0.0523
	2	0.0486	0.9963	0.0037
	3	0.0036	0.9999	0.0001
	4	0.0001	1.0000	0.0000

Cumulative Distribution Function CDF: $F(x)=P(X\le x)$

Example:

$F(3)=P(X \le 3) = P(X=0) + P(X=1) + P(X=2) + P(X=3) = 0.9999$

Complementary Cumulative Distribution Function (tail distribution) or CCDF: $F_{>}(x)=P(X>x)$

Example: $F_{>}(0)= P(X > 0) = 1 - P(X \le 0) = 1 - 0.6561 = 0.3439$

Mean or Expected Value of X

The mean or expected value of the discrete random variable X, denoted as μ or $E(X)$, is

$$\mu = E(X) = \sum_x x \cdot P(X = x) = \sum_x x \cdot f(x)$$

- The mean = the weighted average of all possible values of *X*. It represents its "center of mass"

- The mean may, or may not, be an allowed value of X

- It is also called the arithmetic mean (to distinguish from e.g. the geometric mean discussed later)

- Mean may be infinite if X any integer and tail $P(X=x)>c/x^2$

Outcomes of 6 random experiments

0, 1, 0, 0, 2, 1

$$\text{Mean} = \frac{0+1+0+0+2+1}{6} =$$

$$= \frac{3 \times 0 + 2 \times 1 + 1 \times 2}{6} =$$

$$= 0 \times \frac{3}{6} + 1 \times \frac{2}{6} + 2 \times \frac{1}{6} = \sum_{x=0}^{2} x P(X=x)$$

- $$E[X] = \sum_{x} x \cdot P(X=x)$$
- $$E[X^2] = \sum x^2 \cdot P(X=x)$$
- $$E[a \cdot X + b \cdot X^2] = \sum (ax + bx^2) \times P(X=x) = a \cdot \sum x P(X=x) + b \sum x^2 P(X=x)$$
- $$E[e^X] = \sum e^x P(X=x)$$

Variance $V(X)$: square of a typical deviation from the mean $\mu = E(X)$

$V(X) = \sigma^2$, where σ is called standard deviation

$$\sigma^2 = V(X) = E((X-\mu)^2) =$$
$$= E(X^2 - 2\mu X + \mu^2) = E(X^2) -$$
$$- 2\mu E(X) + \mu^2 = E(X^2) - 2\mu^2 + \mu^2 =$$
$$= E(X^2) - \mu^2 = E(X^2) - (E(X))^2$$

Variance of a Random Variable

If X is a discrete random variable with probability mass function $f(x)$,

$$E\left[h(X)\right]=\sum_x h(x)\cdot P(X=x)=\sum_x h(x)f(x) \qquad (3\text{-}4)$$

If $h(x)=(X-\mu)^2$, then its expectation, $V(x)$, is the variance of X.

$\sigma=\sqrt{V(x)}$, is called standard deviation of X

$$\sigma^2=V(X)=\sum_x (x-\mu)^2 f(x) \text{ is the definitional formula}$$

$$=\sum_x \left(x^2-2\mu x+\mu^2\right)f(x)$$

$$=\sum_x x^2 f(x)-2\mu\sum xf(x)+\mu^2\sum_x f(x)$$

$$=\sum_x x^2 f(x)-2\mu^2+\mu^2$$

$$=\sum_x x^2 f(x)-\mu^2 \text{ is the computational formula}$$

Variance can be infinite
if X can be any integer
and tail of P(X=x) $\geq c/x^3$

Skewness of a random variable

- Want to quantify how asymmetric is the distribution around the mean?
- Need any odd moment: $E[(X-\mu)^{2n+1}]$
- Cannot do it with the first moment: $E[X-\mu]=0$
- Normalized 3-rd moment is skewness: $\gamma 1=E[(X-\mu)^3/\sigma^3]$
- Skewness can be infinite if X takes unbounded integer values and tail $P(X=x) \geq c/x^4$

Geometric mean of a random variable

- Useful for very broad distributions (many orders of magnitude)?
- Mean may be dominated by very unlikely but very large events. Think of a lottery
- Exponent of the mean of *log X*: *Geometric mean=exp(E[log X])*
- Geometric mean usually is not infinite

Summary: Parameters of a Probability Distribution

- Probability Mass Function (PMF): $f(x)=Prob(X=x)$
- Cumulative Distribution Function (CDF): $F(x)=Prob(X\leq x)$
- Complementary Cumulative Distribution Function (CCDF): $F_{>}(x)=Prob(X>x)$
- The mean, $\mu=E[X]$, is a measure of the center of mass of a random variable
- The variance, $V(X)=E[(X-\mu)^2]$, is a measure of the dispersion of a random variable around its mean
- The standard deviation, $\sigma=[V(X)]^{1/2}$, is another measure of the dispersion around mean. Has the same units as X
- The skewness, $\gamma 1=E[(X-\mu)^3/\sigma^3]$, a measure of asymmetry around mean
- The geometric mean, $\exp(E[\log X])$ is useful for very broad distributions