

Grading:

Attendance	10%
Homework	20%
Midterm 1	20%
Midterm 2	20%
Final Exam	30%

Exams:

Midterm 1 (2/24/2026 11am - 2/26/2026 11:59pm)

- Basic concepts of probability and statistics
- Combinatorics
- Bayes theorem
- Discrete probability distributions

Midterm 2 (3/31/2026 11am - 4/02/2026 11:59pm)

- Continuous probability distributions
- Multivariate statistics

Final Exam

- Cumulative: all of the material covered in class

Office Hours

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Everitt Lab 3213

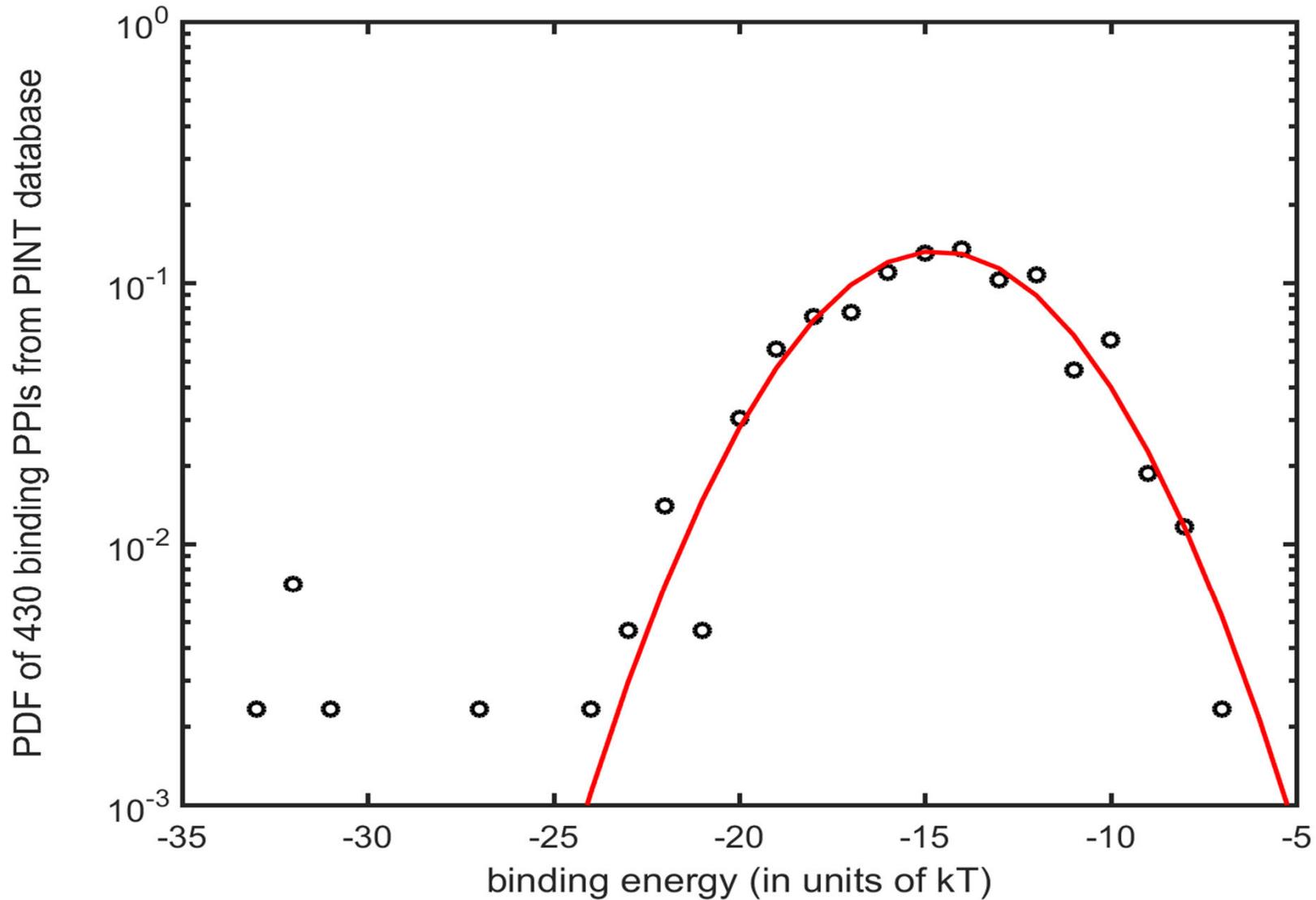
Mondays 5:30PM-6:30PM

Wednesdays 5:30PM-6:30PM

Matlab exercise

- In Matlab load `PINT_binding_energy.mat` with binding energy E_{ij} (in units of kT at room temperature) for 430 pairs of interacting proteins from human, yeast, etc.
- Data collected in 2007 from the PINT database <http://www.bioinfodatabase.com/pint/> and analyzed in J. Zhang, S. Maslov, E. Shakhnovich, *Molecular Systems Biology* (2008)
- Fit Gaussian to the distribution of E_{ij} using `dfittool`
- Use “Exclude” button to generate the new exclusion rule to drop all points with $X < -23$ from the fit
- Use “New Fit” button to generate the new “Normal” fit with the exclusion rule you just created
- Find mean (μ) and standard deviation (σ)
- Select “probability plot” from “Display type” dropdown menu to evaluate the quality of the plot. Where does the probability plot deviate from a straight line?

How does it compare with the experimental data ?



J. Zhang, S. Maslov, E. Shakhnovich,
Nature/EMBO Molecular Systems Biology (2008)

Data on binding interactions
from PINT database

Dissociation constant

- Interaction between two molecules (say, proteins) is usually described in terms of **dissociation constant**

$$K_{ij} = 1M \exp(-E_{ij}/kT)$$

- **Law of Mass Action**: the concentration D_{ij} of a heterodimer formed out of two proteins with free (monomer) concentrations C_i and C_j : $D_{ij} = C_i C_j / K_{ij}$
- What is the distribution of K_{ij} ?
- Answer: it is called log-normal since the **logarithm of K_{ij}** is the **binding energy $-E_{ij}/kT$** which is normally distributed

$$X = Y^2 \text{ or } Y = \sqrt{X}$$

Y - uniform distribution
between $[0, 1]$

$$P(Y < y) = y$$

$$P(X < x) = P(\sqrt{X} < \sqrt{x}) =$$

$$= P(Y < \sqrt{x}) = \sqrt{x}$$

$$\text{Prob. density}(x) = \frac{d}{dx} P(X < x) = \frac{1}{2\sqrt{x}}$$

Let $X = \exp(W)$ and

W is $N(\theta, \omega^2)$

$$P(X > x) = P(W > \ln(x)) =$$

$$= \int_{\ln(x)}^{+\infty} \frac{1}{\sqrt{2\pi}\omega} \exp\left(-\frac{(\ln(y) - \theta)^2}{2\omega^2}\right) d\ln y$$

$$= \int_{\ln(x)}^{+\infty} \frac{1}{\sqrt{2\pi}\omega} \exp\left(-\frac{(\ln(y) - \theta)^2}{2\omega^2}\right) \frac{dy}{y}$$

PDF = $\frac{1}{\sqrt{2\pi}\omega y} \exp\left(-\frac{(\ln y - \theta)^2}{2\omega^2}\right)$

Lognormal Distribution

- Let W denote a normal random variable with mean of θ and variance of ω^2 , i.e., $E(W) = \theta$ and $V(W) = \omega^2$
- As a change of variable, let $X = e^W = \exp(W)$ and $W = \ln(X)$
- Now X is a lognormal random variable.

$$\begin{aligned} F(x) &= P[X \leq x] = P[\exp(W) \leq x] = P[W \leq \ln(x)] \\ &= P\left[Z \leq \frac{\ln(x) - \theta}{\omega}\right] = \Phi\left[\frac{\ln(x) - \theta}{\omega}\right] = \quad \text{for } x > 0 \\ &= 0 \quad \text{for } x \leq 0 \end{aligned}$$

$$f(x) = \frac{dF(x)}{dx} = \frac{1}{x\omega\sqrt{2\pi}} e^{-\left[\frac{\ln(x) - \theta}{2\omega}\right]^2} \quad \text{for } 0 < x < \infty$$

$$E(X) = e^{\theta + \omega^2/2} \quad \text{and} \quad V(X) = e^{2\theta + \omega^2} (e^{\omega^2} - 1) \quad (4-22)$$

Lognormal Graphs

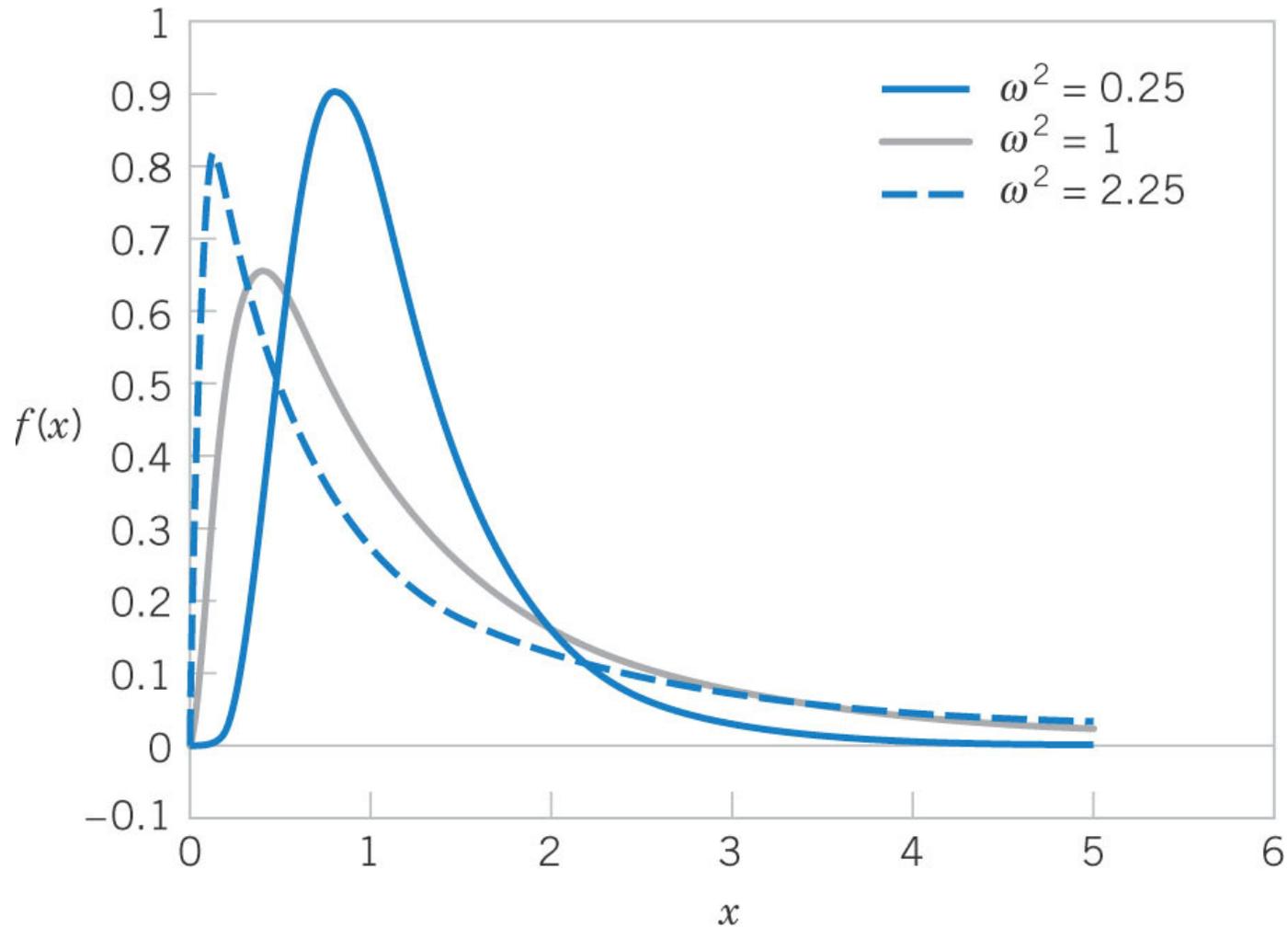


Figure 4-27 Lognormal probability density functions with $\theta = 0$ for selected values of ω^2 .

Credit: XKCD
comics

WHY ARE THERE SLAVES IN THE BIBLE

WHY DO TWINS HAVE DIFFERENT FINGERPRINTS
WHY ARE AMERICANS AFRAID OF DRAGONS

WHY IS HTTPS CROSSED OUT IN RED
WHY IS THERE A LINE THROUGH HTTPS
WHY IS THERE A RED LINE THROUGH HTTPS ON FACEBOOK
WHY IS HTTPS IMPORTANT

QUESTIONS FOUND IN GOOGLE AUTOCOMPLETE



WHY ARE THERE WEEKS
WHY DO I FEEL DIZZY

WHY DO WHALES JUMP
WHY ARE WITCHES GREEN
WHY ARE THERE MIRRORS ABOVE BEDS
WHY DO I SAY UH
WHY IS SEA SALT BETTER
WHY ARE THERE TREES IN THE MIDDLE OF FIELDS
WHY IS THERE NOT A POKEMON MMO
WHY IS THERE LAUGHING IN TV SHOWS
WHY ARE THERE DOORS ON THE FREEWAY
WHY ARE THERE SO MANY SVCHOST.EXE RUNNING
WHY AREN'T THERE ANY COUNTRIES IN ANTARCTICA
WHY ARE THERE SCARY SOUNDS IN MINECRAFT
WHY IS THERE KICKING IN MY STOMACH
WHY ARE THERE TWO SLASHES AFTER HTTP
WHY ARE THERE CELEBRITIES
WHY DO SNAKES EXIST
WHY DO OYSTERS HAVE PEARLS
WHY ARE DUCKS CALLED DUCKS
WHY DO THEY CALL IT THE CLAP
WHY ARE KYLE AND CARTMAN FRIENDS
WHY IS THERE AN ARROW ON AANG'S HEAD
WHY ARE TEXT MESSAGES BLUE
WHY ARE THERE MUSTACHES ON CLOTHES
WHY ARE THERE MUSTACHES ON CARS
WHY ARE THERE MUSTACHES EVERYWHERE
WHY ARE THERE SO MANY BIRDS IN OHIO
WHY IS THERE SO MUCH RAIN IN OHIO
WHY IS OHIO WEATHER SO WEIRD

WHY DO IGUANAS DIE

WHY AREN'T THERE DINOSAUR GHOSTS

WHY ARE THERE MALE AND FEMALE BIKES

WHY ARE THERE TINY SPIDERS IN MY HOUSE

WHY DO SPIDERS COME INSIDE

WHY ARE THERE HUGE SPIDERS IN MY HOUSE

WHY ARE THERE LOTS OF SPIDERS IN MY HOUSE

WHY ARE THERE SPIDERS IN MY ROOM

WHY ARE THERE SO MANY SPIDERS IN MY ROOM

WHY DO SPIDER BITES ITCH

WHY IS DYING SO SCARY

WHY IS THERE NO GPS IN LAPTOPS

WHY DO KNEES CLICK

WHY AREN'T THERE E GRADES

WHY IS ISOLATION BAD

WHY DO BOYS LIKE ME

WHY DON'T BOYS LIKE ME

WHY IS THERE ALWAYS A JAVA UPDATE

WHY ARE THERE RED DOTS ON MY THIGHS

WHY IS LYING GOOD

WHY IS GPS FREE

WHY IS SEX SO IMPORTANT

WHY ARE THERE SWARMS OF GNATS

WHY IS THERE PHLEGM

WHY ARE THERE SO MANY CROWS IN ROCHESTER, MN

WHY IS PSYCHIC WEAK TO BUG

WHY DO CHILDREN GET CANCER

WHY IS POSEIDON ANGRY WITH ODYSSEUS

WHY IS THERE ICE IN SPACE

WHY ARE THERE DOGS AFRAID OF FIREWORKS

WHY IS THERE NO KING IN ENGLAND

WHY ARE CIGARETTES LEGAL

WHY ARE THERE DUCKS IN MY POOL

WHY IS JESUS WHITE

WHY IS THERE LIQUID IN MY EAR

WHY DO Q TIPS FEEL GOOD

WHY DO GOOD PEOPLE DIE

WHY ARE ULTRASOUNDS IMPORTANT

WHY ARE ULTRASOUND MACHINES EXPENSIVE

WHY IS STEALING WRONG

WHY AREN'T THERE ANY FOREIGN MILITARY BASES IN AMERICA

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Multiple random variables, Correlations

What we learned so far...

- **Random Events:**
 - Working with **events as sets**: union, intersection, etc.
 - Some events are simple: Head vs Tails, Cancer vs Healthy
 - Some are more complex: $10 < \text{Gene expression} < 100$
 - Some are even more complex: Series of dice rolls: 1,3,5,3,2
 - **Conditional probability**: $P(A|B) = P(A \cap B) / P(B)$
 - **Independent events**: $P(A|B) = P(A)$ or $P(A \cap B) = P(A) * P(B)$
 - **Bayes theorem**: relates $P(A|B)$ to $P(B|A)$
- **Random variables:**
 - **Mean, Variance, Standard deviation**. How to work with $E(g(X))$
 - **Discrete** (Uniform, Bernoulli, Binomial, Poisson, Geometric, Negative binomial, Power law);
PMF: $f(x) = \text{Prob}(X=x)$; **CDF**: $F(x) = \text{Prob}(X \leq x)$;
 - **Continuous** (Uniform, Exponential, Erlang, Gamma, Normal, Log-normal);
PDF: $f(x)$ such that $\text{Prob}(X \text{ inside } A) = \int_A f(x) dx$; **CDF**: $F(x) = \text{Prob}(X \leq x)$
- **Next step**: work with **multiple random variables** measured together in the same series of random experiments

Concept of Joint Probabilities

- Biological systems are usually described not by a single random variable but by **many random variables**
- Example: The expression state of a human cell: 20,000 random variables X_i for each of its genes
- A **joint probability distribution** describes the behavior of **several random variables**
- We will start with just two random variables X and Y and generalize when necessary

Joint Probability Mass Function Defined

The **joint probability mass function** of the **discrete random variables** X and Y , denoted as $f_{XY}(x, y)$, satisfies:

(1) $f_{XY}(x, y) = P(X=x, Y=y)$

(2) $f_{XY}(x, y) \geq 0$ All probabilities are non-negative

(3) $\sum_x \sum_y f_{XY}(x, y) = 1$ The sum of all probabilities is 1

Montgomery Runger 5th edition Equation (5-1)

Example 5-1: # Repeats vs. Signal Bars

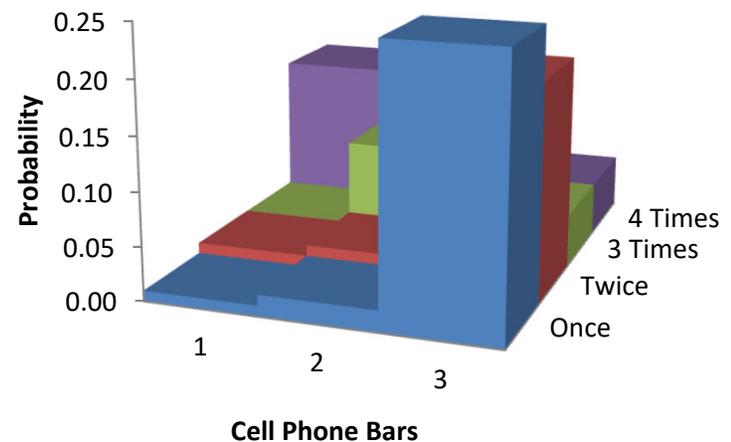
You use your cell phone to check your airline reservation. It asks you to speak the name of your departure city to the voice recognition system.

- Let Y denote the number of times you have to state your departure city.
- Let X denote the number of bars of signal strength on you cell phone.

y = number of times city name is stated	x = number of bars of signal strength		
	1	2	3
1	0.01	0.02	0.25
2	0.02	0.03	0.20
3	0.02	0.10	0.05
4	0.15	0.10	0.05

Figure 5-1 Joint probability distribution of X and Y . The table cells are the probabilities. Observe that more bars relate to less repeating.

Bar Chart of Number of Repeats vs. Cell Phone Bars



Marginal Probability Distributions (discrete)

For a **discrete** joint PDF, there are **marginal distributions** for **each random variable**, formed by summing the joint PMF over the other variable.

$$f_X(x) = \sum_y f_{XY}(x, y)$$

$$f_Y(y) = \sum_x f_{XY}(x, y)$$

y = number of times city name is stated	x = number of bars of signal strength			$f_Y(y) =$
	1	2	3	
1	0.01	0.02	0.25	0.28
2	0.02	0.03	0.20	0.25
3	0.02	0.10	0.05	0.17
4	0.15	0.10	0.05	0.30
$f_X(x) =$	0.20	0.25	0.55	1.00

Called **marginal** because they are **written in the margins**

Figure 5-6 From the prior example, the joint PMF is shown in green while the two marginal PMFs are shown in purple.

Conditional Probability Distributions

Recall that $P(B|A) = \frac{P(A \cap B)}{P(A)}$

$$P(Y=y | X=x) = P(X=x, Y=y) / P(X=x) = f(x, y) / f_X(x)$$

From Example 5-1

$$P(Y=1 | X=3) = 0.25/0.55 = 0.455$$

$$P(Y=2 | X=3) = 0.20/0.55 = 0.364$$

$$P(Y=3 | X=3) = 0.05/0.55 = 0.091$$

$$P(Y=4 | X=3) = 0.05/0.55 = 0.091$$

$$\text{Sum} = 1.00$$

y = number of times city name is stated	x = number of bars of signal strength			$f_Y(y) =$
	1	2	3	
1	0.01	0.02	0.25	0.28
2	0.02	0.03	0.20	0.25
3	0.02	0.10	0.05	0.17
4	0.15	0.10	0.05	0.30
$f_X(x) =$	0.20	0.25	0.55	1.00

Note that there are 12 probabilities conditional on X , and 12 more probabilities conditional upon Y .

X and Y are Bernoulli variables

	Y=0	Y=1
X=0	2/6	1/6
X=1	2/6	1/6

What is the marginal $P_Y(Y=0)$?

A. 1/6

B. 2/6

C. 3/6

D. 4/6

E. I don't know

Get your i-clickers

X and Y are Bernoulli variables

	Y=0	Y=1
X=0	2/6	1/6
X=1	2/6	1/6

What is the conditional $P(X=0 | Y=1)$?

A. 2/6

B. 1/2

C. 1/6

D. 4/6

E. I don't know

Get your i-clickers